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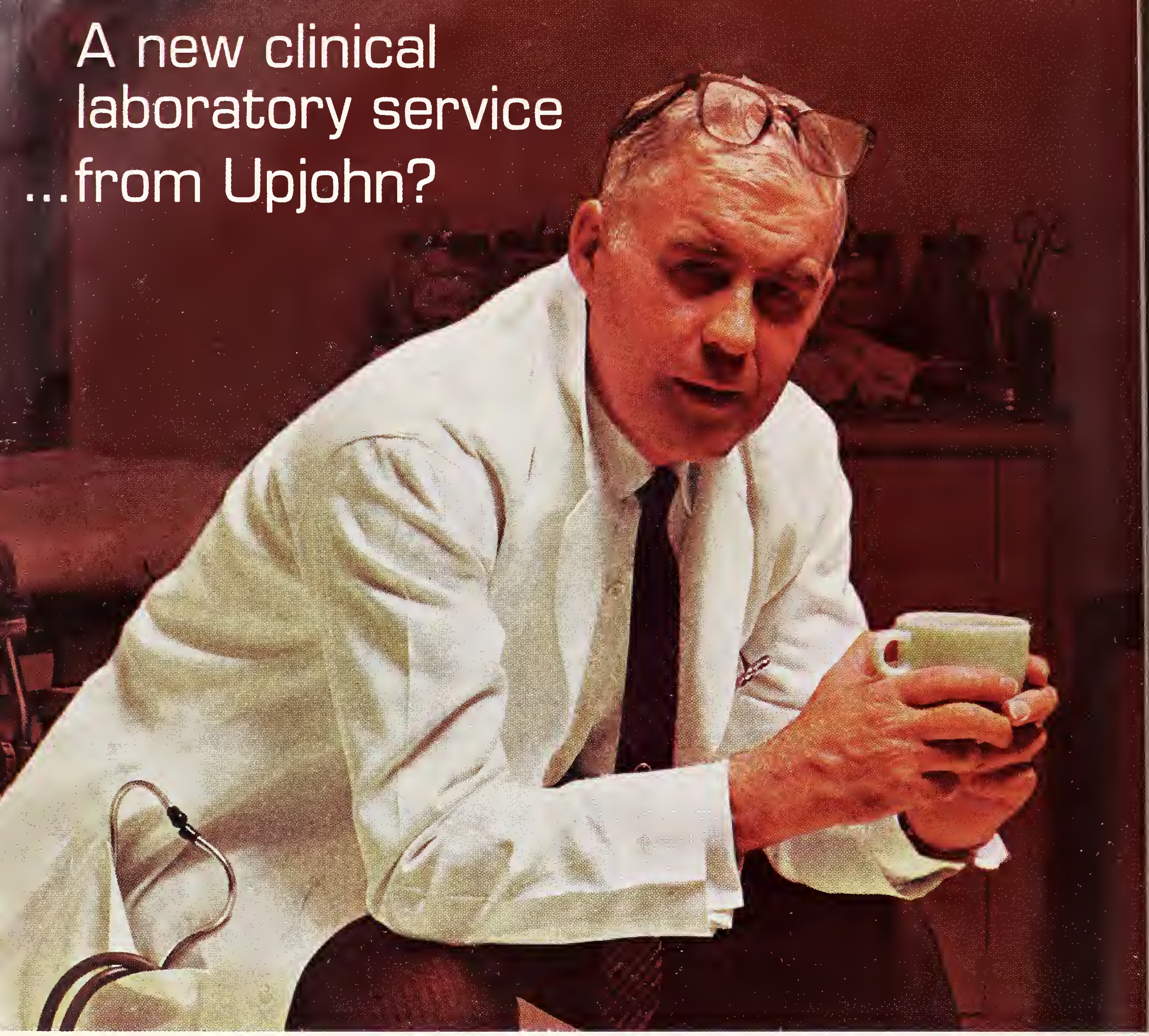
A new clinical laboratory service ...from Upjohn?



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TABLETS & GRANULES

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■ for fever blisters and canker sores of herpetic origin

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Lactinex has been shown to be useful in the treatment of gastrointestinal disturbances, and for relieving the painful oral lesions of fever blisters and canker sores of herpetic origin.[1,2,3,4,5,6,7,8]

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Literature on indications and dosage available on request.

HYNSON, WESTCOTT & DUNNING, INC.

Baltimore, Maryland 21201

(LX-05)

References:

(1) Siver, R. H.: CMD, *21*:109, September 1954. (2) Frykman, H. H.: Minn. Med., *38*:19-27, January 1955. (3) McGivney, J.: Tex. State Jour. Med., *51*:16-18, January 1955. (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., *15*:15-16, October 1965. (5) Weekes, D. J.: N.Y. State Jour. Med., *58*:2672-2673, August 1958. (6) Weekes, D. J.: EENT Digest, *25*:47-59, December 1963. (7) Abbott, P. L.: Jour. Oral Surg., Anes., & Hosp. Dental Serv., 310-312, July 1961. (8) Rapoport, L. and Levine, W. I.: Oral Surg., Oral Med. & Oral Path., *20*:591-593, November 1965.

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Paraflex® (chlorzoxazone)* 250 mg.
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Parafon Forte tablets help to relieve pain, restore mobility . . . stop pain-spasm feedback

by providing:

a nonsalicylate analgesic equal to aspirin for the relief of pain,[1,2] yet unlikely to produce the irritation to the gastric mucosa so often associated with salicylate therapy[3]

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References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth, J. L. A., *et al.*: Gastroenterology *44*:146, 1963. 4. Berman, H. H., *et al.*: Dis. Nerv. Syst. *25*:430, 1964. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

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*U.S. PATENT NO. 2,895,877

JULY, 1969/VOL. 26, NO. 7

ARIZONA MEDICINE

JOURNAL OF ARIZONA MEDICAL ASSOCIATION • MEDICAL SOCIETY OF THE UNITED STATES AND MEXICO

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Published monthly by The Arizona Medical Association, Inc., with offices at 4601 N. Scottsdale Rd., Suite 201, Scottsdale, Arizona 85251. Subscription $5 a year, single copy 50 cents. Second class postage paid at Scottsdale, Arizona, and at additional mailing offices.

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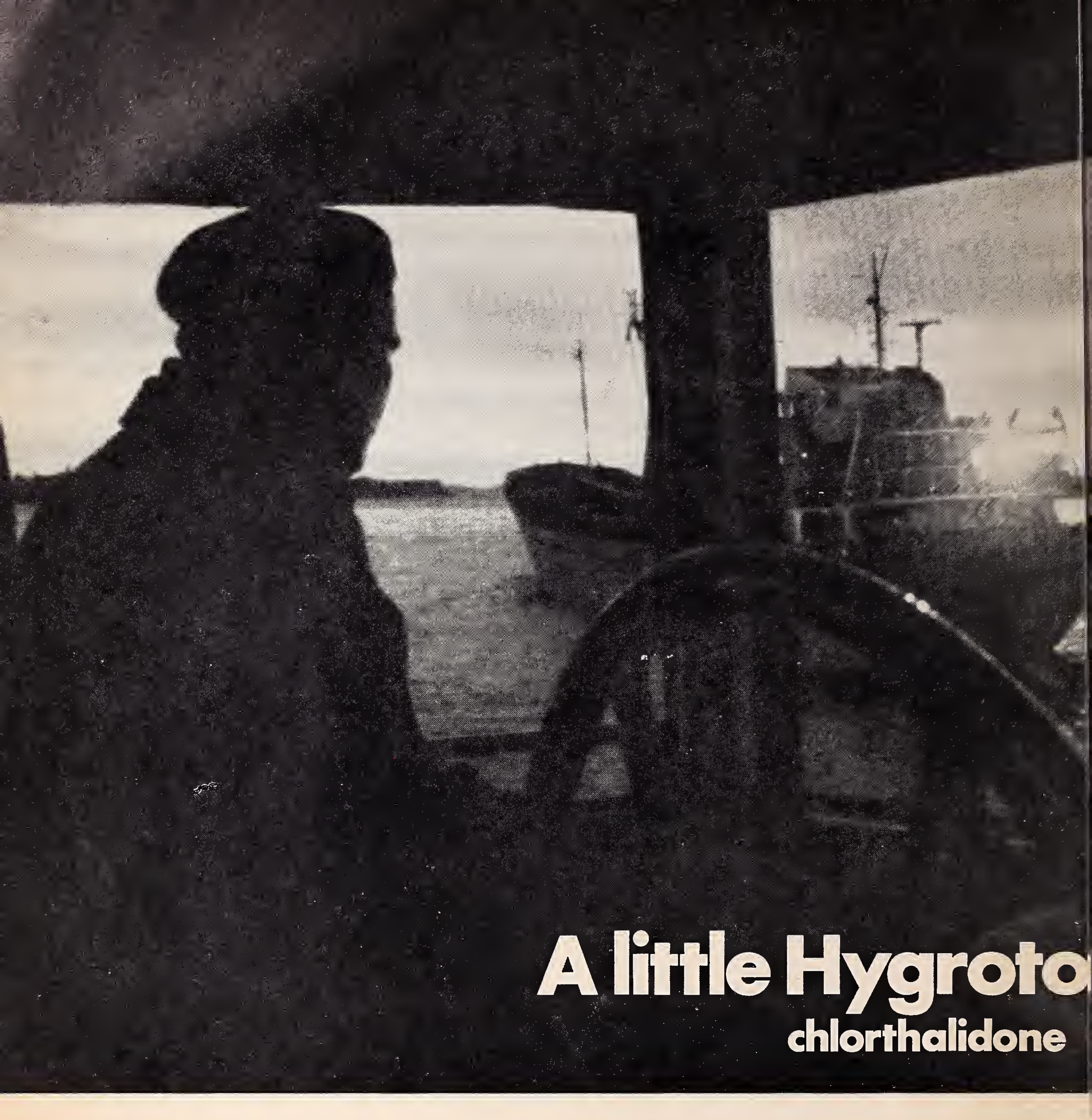

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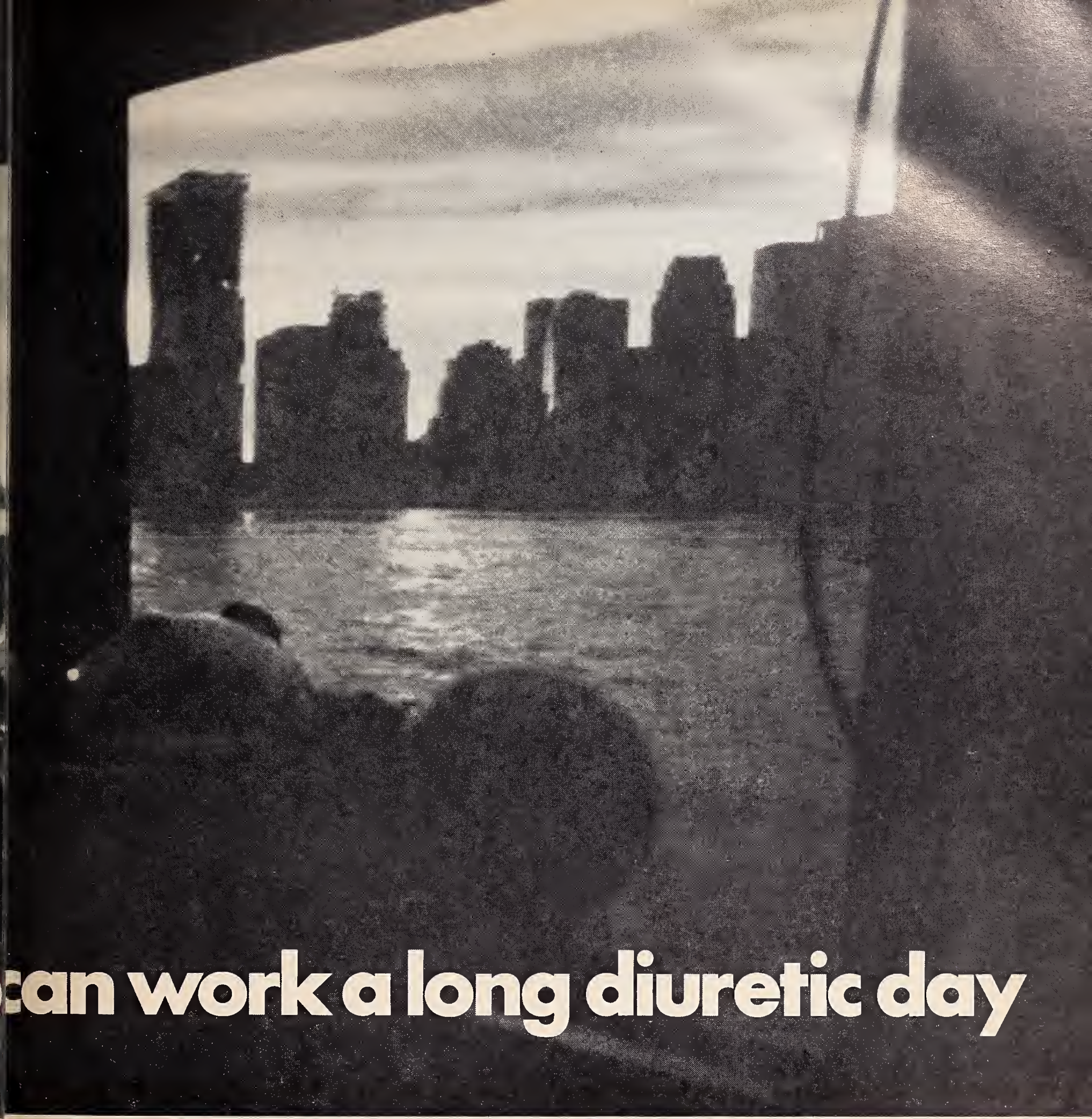

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Editor's Page

PESTILENT VAPOURS

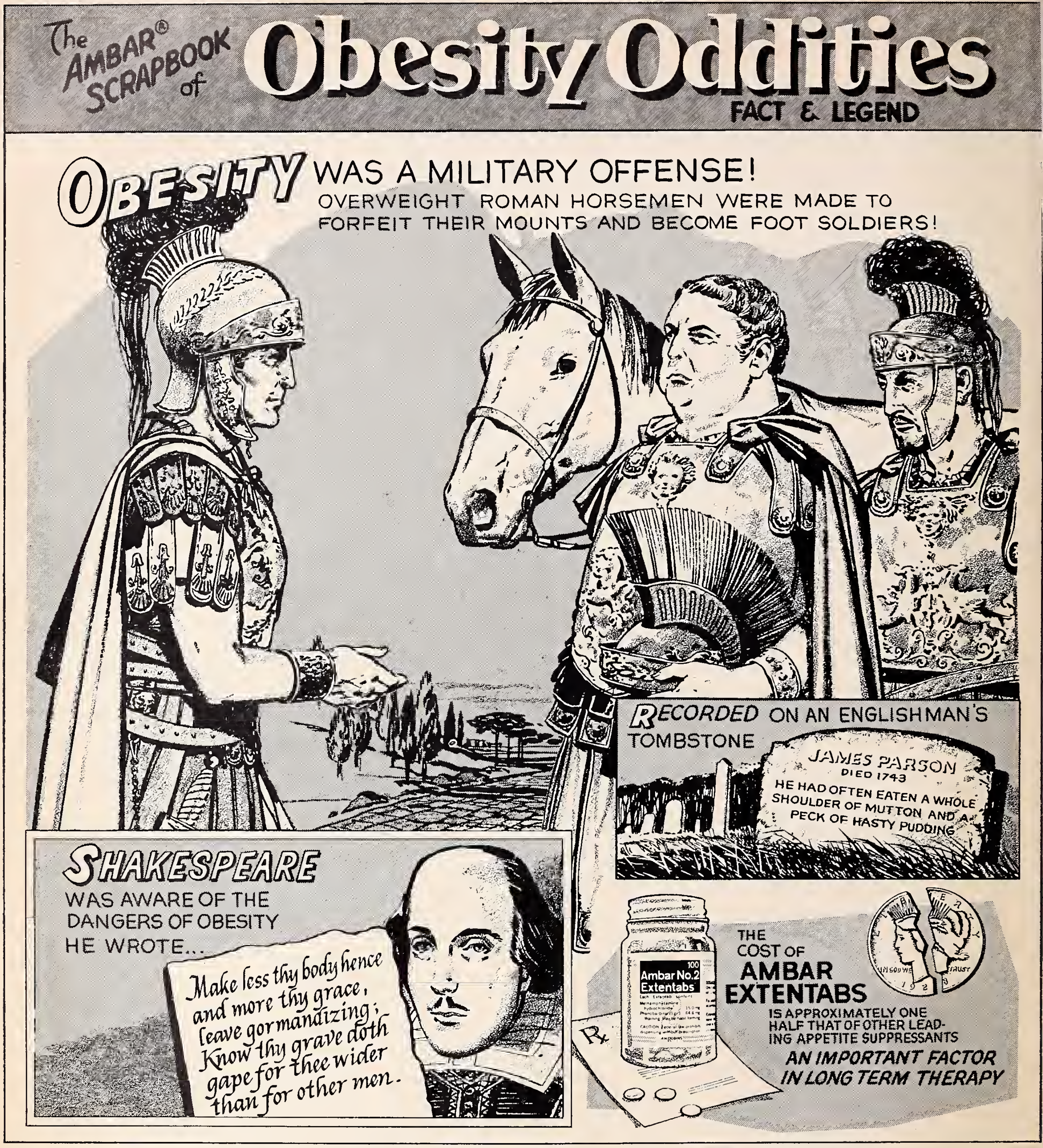
Hamlet described our atmosphere as: "This most excellent canopy, the air, this brave o'erhanging firmament . . . appeareth nothing to me but a foul and pestilent congregation of vapours." This description might aptly be applied to some of the air of our larger cities, polluted by exhaust gases, dust, and industrial by-products. A recent issue of the "Royal Bank of Canada Monthly Letter" presented evidence that within twenty years life on our planet will be showing signs of succumbing to pollution. This disaster is already plaguing some of our streams and lakes such as Lake Erie, which has developed large expanses of dead water as a result of uncontrolled pollution.

There is a tendency for the general public to assume that the human race will somehow "muddle through," as it has in past social, environmental, and economic crises. As population grows by logarithmic measure, and as our terrestial satellite becomes correspondingly less spacious, the chance of "muddling through" the pollution problem grows less.

The A.M.A. has taken an increasing part in pointing out the health hazards of continued uncontrolled pollution of our natural resources. At its sixth annual Congress on Environmental Health, the subject of "Noise Pollution" was cited as not only an inconvenience but a physical and psychological hazard.

The medical community can play a role in several areas of the problem. The private physician can act as liaison between the public, and industrial engineers. The doctor can encourage private efforts and legislation, such as the recent anti-smog bill, where necessary. He can help to educate and increase public awareness of the problem by both private and public comments, and by passing appropriate resolutions at the Annual State Meeting. Arizona Physicians can lead the way in the battle to prevent Arizona's, ". . . excellent canopy . . .," from becoming truly, ". . . a foul and pestilent congregation of vapours."

Robert F. Lorenzen, M.D.
Editor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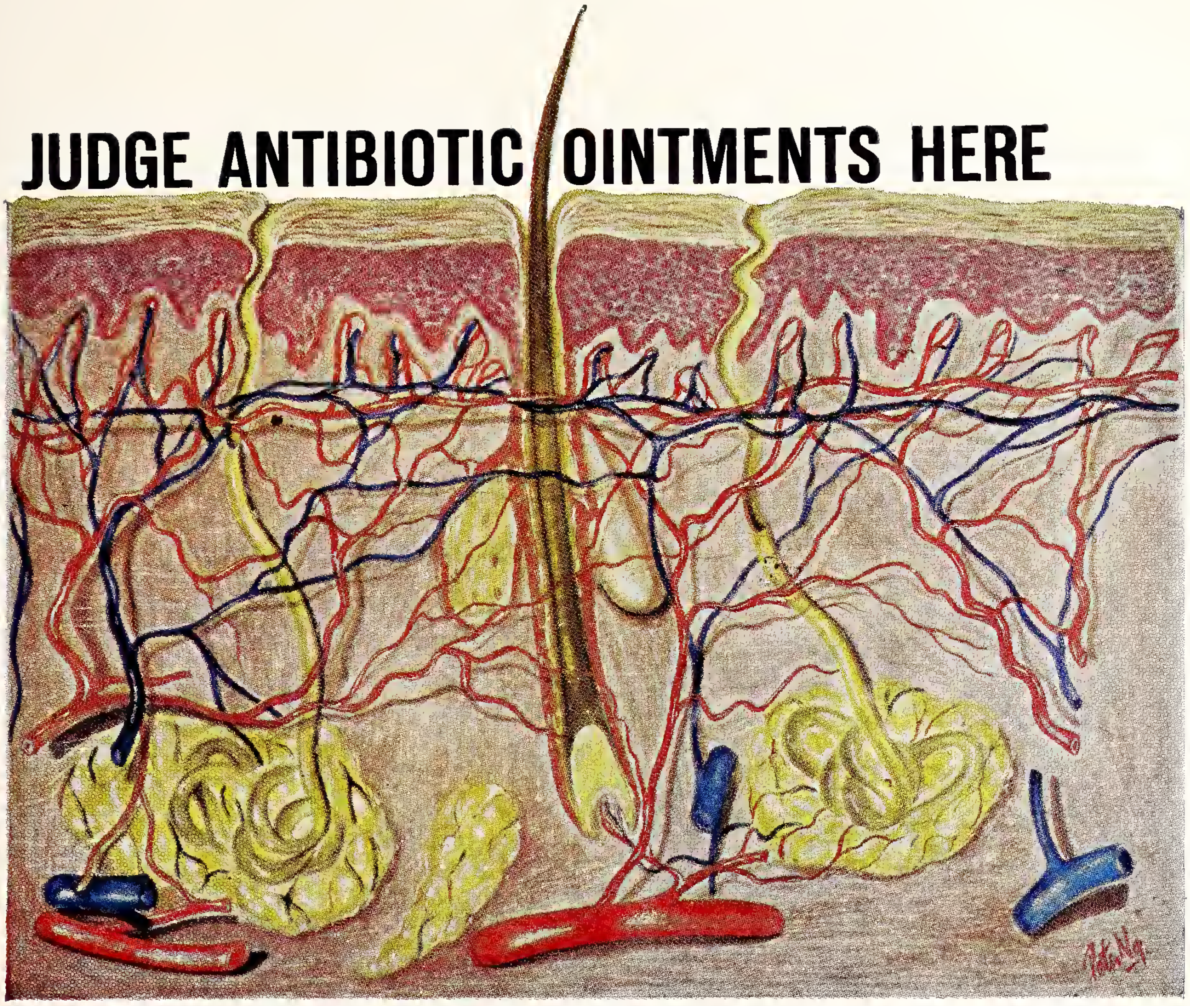

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Contraindications: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

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Priscoline®
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could help

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Now he's about to get a cold shoulder too.

His next step should be Priscoline. It dilates peripheral blood vessels, increases blood flow to extremities. Helps relieve numbness and chill associated with PVD.

And Priscoline helps patients prone to claudication move around—makes walking less painful.

Priscoline could help this country gentleman warm his feet. If not her heart.

Please turn page for prescribing information on Priscoline, oral peripheral vasodilator.

CIBA

Priscoline® hydrochloride
(tolazoline hydrochloride)
Oral Peripheral Vasodilator

INDICATIONS
Spastic peripheral vascular disorders.
PRECAUTIONS
Priscoline stimulates gastric activity and increases hydrochloric acid content of the stomach; use cautiously in patients with gastritis or peptic ulcer or in those with suspected peptic ulcer. Give cautiously, if at all, to patients with known or suspected coronary artery disease.
ADVERSE REACTIONS
Occasional: nausea, epigastric discomfort, tachycardia, flushing, slight rise or fall in blood pressure, increased pilomotor activity with tingling or chilliness. Rare: vomiting, diarrhea. Symptoms are generally mild and frequently disappear with continued therapy, regardless of dosage.
DOSAGE
Careful individualization of dosage is required.
Tablets: Usually 25 mg 4 to 6 times daily is sufficient. If necessary dosage may be increased gradually up to 50 mg 6 times daily.
Lontabs: Generally, 1 Lontab every 12 hours will achieve the same effect as one 25-mg regular tablet every 4 hours (6 times a day). Thus, continuous action throughout the night is achieved without the need for arising to take additional medication.
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Lontabs, 80 mg (bright yellow); bottles of 100.
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Material submitted for publication in ARIZONA MEDICINE should conform to the following policies:

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2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

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4. Articles are accepted for publication only if they are contributed exclusively to this Journal. Ordinarily, contributors will be notified within 60 days if a manuscript is accepted for publication. Every effort will be made to return unused manuscripts.

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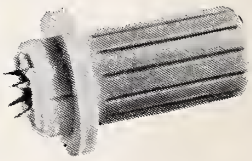

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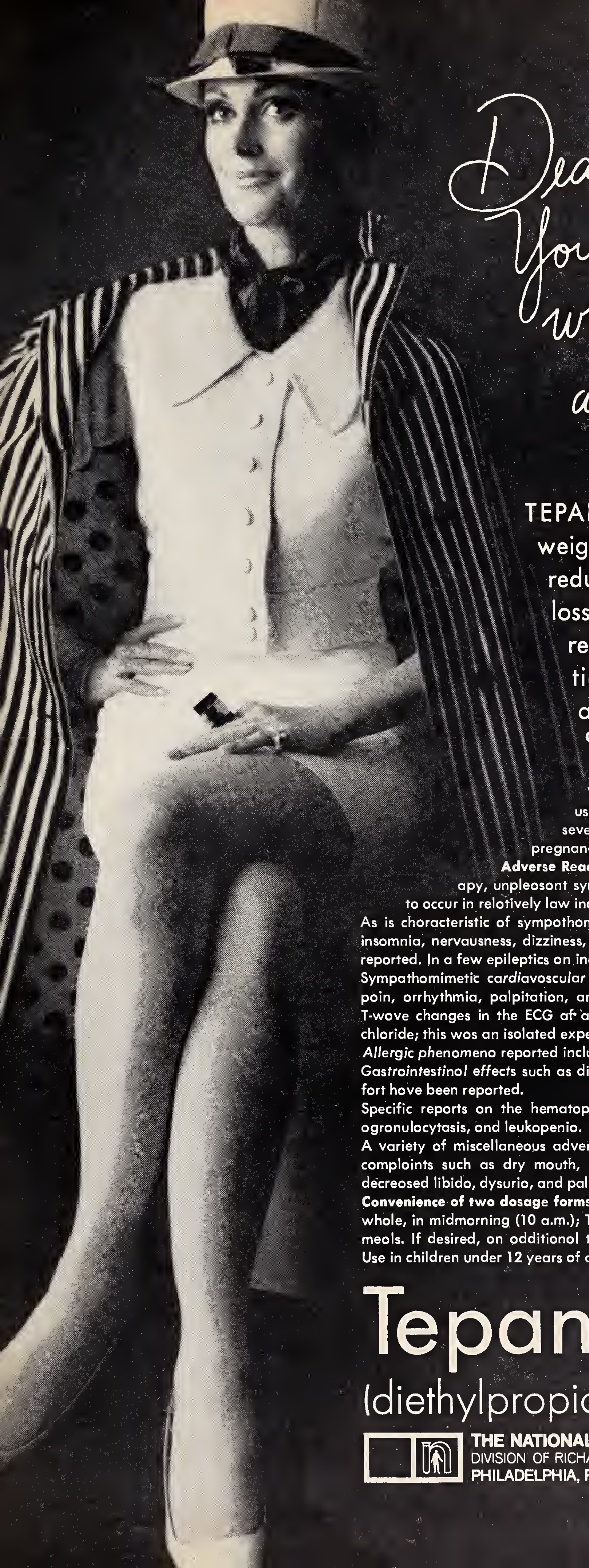

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As is characteristic of sympathomimetic agents, it may occasionally cause *CNS effects* such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptics an increase in convulsive episodes has been reported.

Sympathomimetic *cardiovascular effects* reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others.

Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema. *Gastrointestinal effects* such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported.

Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia.

A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

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Tepanil® Ten-tab®
(continuous release form)
(diethylpropion hydrochloride)

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON-MERRELL INC.
PHILADELPHIA, PENNSYLVANIA 19144 T-918A U.S. PATENT NO. 3,001,910 5/69

They don't feel they "suffer" from hypertension...

that's the "Buti" part of Butiserpazide.

The "Buti" part of BUTISERPAZIDE—the mildly sedative action of BUTISOL acting in concert with the classic thiazide/reserpine formula—proved helpful in one study in reducing hypertensive symptoms in over half the patients.[1]

Among the symptoms showing "striking" overall improvement were headache, nervousness, palpitation and dizziness. Nor is that all there is to the "beauty" of BUTISERPAZIDE. Clinical comparisons have also shown that many patients respond with smooth, uniform lowering of blood pressure[2]... at times *below* the levels achieved with previous therapy[1,2]... as well as a lowered incidence of drug side effects. (The usual dosage is just 1 tablet once or twice a day.)

You have a choice of 2 strengths:

Butiserpazide®-25

PRESTABS®* Tablets
BUTISOL® (butabarbital) 30 mg.†; hydrochlorothiazide 25 mg.; reserpine 0.1 mg.

Butiserpazide®-50

PRESTABS®* Tablets
BUTISOL® (butabarbital) 30 mg.†; hydrochlorothiazide 50 mg.; reserpine 0.1 mg.

Lowers blood pressure so smoothly that patients are often untroubled by either the disease...or therapy

Contraindications: Sensitivity to any component, porphyria, peptic ulcer, ulcerative colitis, mental depression, renal impairment or shutdown. **Warnings:** Consider the possibility of sensitivity reactions in patients with history of allergy or bronchial asthma. Coated potassium tablets, sometimes administered in conjunction with antihypertensive therapy, may be associated with small bowel lesions, which have led to obstruction, hemorrhage and perforation. Surgery has frequently been required and deaths have occurred. Such tablets should be used only when indicated and when adequate dietary supplementation is not practical. They should be discontinued immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occur. *Use in Pregnancy:* Exercise caution, since thiazides cross the placental barrier and may cause fetal or neonatal hyperbilirubinemia, thrombocytopenia or altered carbohydrate metabolism; adverse reactions seen in the adult may occur in the newborn. Use reserpine in women of childbearing age only when essential to patient welfare. Increased respiratory secretions, nasal congestion, cyanosis, and anorexia may occur in infants born to reserpine-treated mothers. **Precautions:** *Butisol* (butabarbital)—Exercise caution in moderate to severe hepatic disease. Elderly or debilitated patients may react with marked excitement or depression. *Hydrochlorothiazide*—May induce electrolyte imbalance; when used with digitalis or one of its glycosides and in patients with severe hepatic insufficiency, cardiac arrhythmias or symptoms of impending hepatic coma may occur. Discontinue and institute appropriate countermeasures if prolonged use produces hypokalemia or (likely with sodium restriction) hyponatremia and hypochloremic alkalosis. (Ammonium chloride, used to reverse hypochloremic alkalosis, is contraindicated in hepatic disease.) May produce elevated serum uric acid levels (and, infrequently, gout) or reduce glucose tolerance, altering insulin requirements in diabetics. *Reserpine*—Observe for signs or symptoms of peptic ulcer or ulcerative colitis. Discontinue at first sign of mental depression; keep in mind possibility of suicide. Exercise extreme caution in history of mental depression. May produce cardiac arrhythmias when used with digitalis and quinidine, or may precipitate biliary colic in patients with gallstones. Discontinue 1 to 2 weeks before surgery; inform the anesthetist in event of emergency surgery. Exercise caution in history of epilepsy. Discontinue 1 to 2 weeks before ECT. *General*—Exercise caution in coronary artery disease. **Adverse Reactions:** Dizziness, drowsiness, weakness, nasal congestion, leg cramps, nausea, palpitations, superficial skin bruises, palmar erythema, headache, dehydration, skin rash, "hangover," systemic disturbances, diarrhea, itching, vomiting, paresthesia, photosensitivity, pancreatitis, jaundice, xanthopsia, purpura, thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, anorexia, gastric irritation, abdominal cramping, constipation, glycosuria, vertigo, cutaneous vasculitis, orthostatic hypotension (potentiated by alcohol, barbiturates, or narcotics), increased salivation and gastric secretion, increased intestinal motility, loose stools, angina-like syndrome, arrhythmias, bradycardia, flushing, hypotension, nervousness, paradoxical anxiety, rarely atypical Parkinsonian syndrome, central nervous system sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, optic atrophy), dryness of mouth, syncope, epistaxis, weight gain, and impotence or decreased libido. **Usual Adult Dosage:** BUTISERPAZIDE®-25 or BUTISERPAZIDE®-50: 1 tablet daily or b.i.d. When used with other antihypertensive agents reduce dosage of both drugs about 50% and observe carefully for changes in blood pressure. *Before prescribing or administering, see package insert.* **References:** 1. Coodley, E. L.: Curr. Ther Res 4.460 (Sept.) 1962. 2. Johnson, H. J., Jr.: Penn. Med. J. 67.35 (May) 1964.

†Warning: May be habit forming.

*15 mg. of BUTISOL (butabarbital), plus the other ingredients, in outer layer; 15 mg. of BUTISOL in a specially coated core for delayed release, to approximately equalize duration of action for all components.

McNEIL

McNeil Laboratories, Inc.
Fort Washington, Pa. 19034

Photo professionally posed.

No injection after all!

This penicillin produces high, fast levels—orally.

Pen•Vee® K is usually so rapidly and completely absorbed that therapeutic penicillin levels are attained within 15 to 30 minutes. Thus it can often obviate the need for penicillin injections. The higher serum levels produced generally last longer than with those of oral penicillin G.

Indications: Infections susceptible to oral penicillin G: prophylaxis and treatment of streptococcal infections; treatment of pneumococcal, gonococcal, and susceptible staphylococcal infections; prophylaxis of rheumatic fever in patients with a previous history of the disease.
Contraindications: Infections caused by nonsusceptible organisms; history of penicillin sensitivity.
Warnings: Acute anaphylaxis (may prove fatal unless promptly controlled) is rare but more frequent in patients with previous penicillin sensitivity, bronchial asthma or other allergies. Resuscitative (epinephrine, aminophylline, pressor amines) and supportive (antihistamines, methylprednisolone sodium succinate) drugs should be readily available. Other rare hypersensitivity reactions include nephropathy, hemolytic anemia, leucopenia and thrombocytopenia. In suspected hypersensitivity, evaluation of renal and hematopoietic systems is recommended.
Precautions: In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.
Adverse Reactions: (Penicillin has significant index of sensitization): Skin rashes, ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; serum sickness-like reactions, including chills, fever, edema, arthralgia and prostration. Severe and often fatal anaphylaxis has been reported (see "Warnings").
Composition: Tablets—125 mg. (200,000 units), 250 mg. (400,000 units), 500 mg. (800,000 units); Liquid—125 mg. (200,000 units) and 250 mg. (400,000 units) per 5 cc.

Wyeth Laboratories Philadelphia, Pa.

ORAL PEN•VEE® K

(potassium phenoxymethyl penicillin) Wyeth®

introducing alginates to antacids

for a difference in taste you can feel

Derived from seaweed, and long used to impart velvety consistency to foods, alginates—a Warner-Chilcott contribution to antacid palatability—help 1) erase the chalkiness and grittiness found with some other antacids; 2) dispel unpleasant aftertaste. Like ice cream, Gelusil-M is smooth and creamy; and it has a cool mint flavor. Thus, for your patients Gelusil-M is excellent to start on and easy to stay on.

introducing

GELUSIL®-M

NEW

each 5 ml. teaspoonful contains:
500 mg. magnesium trisilicate
250 mg. aluminum hydroxide (Warner-Chilcott)
200 mg. magnesium hydroxide
*U.S. Patent No. 3,326,755

a consistent buffering anticostive† antacid

†Avoids constipation.

See next page for prescribing information ▶

GELUSIL–one name to remember...and a dosage form for every patient

Gelusil®-M Liquid

Indications: Gelusil-M is indicated for prompt and dependable symptomatic relief of peptic ulcer, gastritis, heartburn, hiatal hernia, esophagitis, and other conditions for which control of gastric hyperacidity is required.

Precaution: Prolonged or intensive therapy in patients with severe renal insufficiency may lead to hypermagnesemia.

Dosage: One to two teaspoonfuls (5 ml. to 10 ml.) between meals and at bedtime or whenever symptoms occur. Certain conditions, such as acute peptic ulcer, may require individualized dosage. If diarrhea occurs, reduce dosage or discontinue use.

Supplied: Gelusil-M (spearmint-flavored)—light green bottles of 12 fl. oz.; and a **special hospital pack.** Keep tightly closed—shake vigorously.

Gelusil® Tablets

Easy to take along / easy to take / pleasantly mint-flavored. An antacid with adsorbent and demulcent properties which contains in one tablet: 0.25 Gm. aluminum hydroxide (Warner-Chilcott) and 0.5 Gm. magnesium trisilicate (USP).

Dosage: 2 tablets—or more—between meals and at bedtime, or whenever symptoms occur. Tablets should be chewed.

Regular Gelusil® Liquid

Pleasant mint flavor...ideal for hospital or home. Available in 12 fl. oz. and 6 fl. oz. bottles and a special hospital pack. An antacid which contains adsorbent and demulcent agents in each 4 ml. teaspoonful: 0.25 Gm. aluminum hydroxide (Warner-Chilcott), 0.5 Gm. magnesium trisilicate (USP).

Dosage: 2 teaspoonfuls (4 ml. each)—or more—between meals and at bedtime, or whenever symptoms occur.

Also Available: Gelusil® Flavor-Pack, Gelusil-Lac®.

WARNER-CHILCOTT
Morris Plains, New Jersey

GM-IN-91-4C

In the complex picture of moderate to severe anxiety...

there is a new reason for prescribing Mellaril (Thioridazine HCl)

effectiveness in mixed anxiety-depression

Long recognized for its usefulness in the treatment of moderate to severe anxiety, Mellaril is now also known to be effective against mixed anxiety-depression.

Often the symptoms of anxiety states are difficult to sort out—even with the most careful probing. The patient may manifest symptoms of agitation, restlessness, insomnia, somatic complaints. But what of the depression that may be mixed in the total picture? It is reassuring to know that Mellaril may be prescribed—with strong possibilities of success—when there is anxiety alone or a mixture of anxiety and depression.

Before prescribing or administering, see Sandoz literature for full product information, including adverse reactions reported with phenothiazines. The following is a brief precautionary statement.
Contraindications: Severe central nervous system depression, comatose states from any cause, hypertensive or hypotensive heart disease of extreme degree.
Warnings: Administer cautiously to patients who have previously exhibited a hypersensitivity reaction (e.g., blood dyscrasias, jaundice) to phenothiazines. Phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus insecticides. During pregnancy, administer only when necessary.
Precautions: There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures. In epileptic patients, anticonvulsant medication should also be maintained. Pigmentary retinopathy may be avoided by remaining within the recommended limits of dosage. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving). Orthostatic hypotension is more common in females than in males. Do not use epinephrine in treating drug-induced hypotension. Daily doses in excess of 300 mg. should be used only in severe neuropsychiatric conditions.
Adverse Reactions: *Central Nervous System*—Drowsiness, especially with large doses, early in treatment; infrequently, pseudoparkinsonism and other extrapyramidal symptoms; nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. *Autonomic Nervous System*—Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. *Endocrine System*—Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. *Skin*—Dermatitis and skin eruptions of the urticarial type, photosensitivity. *Cardiovascular System*—Changes in the terminal portion of the electrocardiogram have been observed in some patients receiving the phenothiazine tranquilizers, including Mellaril (thioridazine hydrochloride). While there is no evidence at present that these changes are in any way precursors of any significant disturbance of cardiac rhythm, several sudden and unexpected deaths apparently due to cardiac arrest have occurred in patients previously showing electrocardiographic changes. The use of periodic electrocardiograms has been proposed but would appear to be of questionable value as a predictive device. *Other*—A single case described as parotid swelling.

Mellaril®
(Thioridazine HCl)
25 mg. t.i.d.

for moderate to severe anxiety and mixed anxiety-depression

SANDOZ SANDOZ PHARMACEUTICALS, HANOVER, N. J. 68-169

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BY-LAWS ....Mrs. Donald D. Ewing (Carol)
810 North Shepherd Hills, Tucson 85710

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CONVENTION ....Mrs. James Hopkins (Patricia)
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FINANCE ....Mrs. Richard J. Toll (Ann)
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HAMER EDUCATION LOAN FUND. .Mrs. Alvin L. Swenson (Vicki)
5250 N. Bartlett Cir., Phoenix

HEALTH CAREERS ....Mrs. Thomas M. Foreman (Teddy)
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HISTORIAN ....Mrs. Melvin Phillips (Jean)
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INTERNATIONAL HEALTH ...Mrs. Joseph B. McNally (Susie)
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LEGISLATION ....Mrs. W. Curtis N. Wilcox (Doris Ann)
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MEMBERSHIP ....Mrs. Charles E. Henderson (Nancy)
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SAFETY-DISASTER PREPAREDNESS:
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352 West Berridge Lane, Phoenix 85013

WA-SAMA ....Mrs. Ruben Acosta (Mary)
3481 E. Edgemont, Tucson 85716

ArMA Reports

THE FOLLOWING ARE THE RESOLUTIONS ACTED UPON BY THE HOUSE OF DELEGATES ON APRIL 26, 1969

RESOLUTION NO. 1

Introduced by Board of Directors, The Arizona Medical Association, Inc.

Subject — 1970 Calendar Year Budget of Income and Expenditures.

WHEREAS, it is customary for the House of Delegates to approve the Budget of Income and Expenditures for the next succeeding calendar year of the Arizona Medical Association, Inc.; therefore be it

RESOLVED, that the following Budget of Income and Expenditures for the calendar year 1970, be adopted as follows:

INCOME:			
400	GENERAL FUND		$162,255.00
401	Association Dues — Active Members	$148,300.00	
401a	Association Dues — Service Members	1,900.00	
402	Sale of Supplies	300.00	
403	AMA Commissions	1,000.00	
404	Interest — Investment Account	6,000.00	
405	Miscellaneous	25.00	
406	BOMEX Rental	4,730.00	
420	PUBLISHING COMMITTEE		$ 44,875.00
421	Advertising	5 35,000.00	
422	Subscriptions, Non-member	450.00	
423	Reprints & Engravings	2,000.00	
424	Other	10.00	
425	Subscriptions, Members	7,415.00	
430	ANNUAL MEETING		$ 26,950.00
430	Total Income	$ 26,950.00	
	TOTAL ANTICIPATED 1970 INCOME		$234,080.00
EXPENDITURES:			
500	GENERAL FUND		$114,980.00
501	Salaries	$ 60,400.00	
502	Payroll Taxes	2,500.00	
503	Meeting Expenses	5,500.00	
504	Travel	4,500.00	
505	Building Operation	11,270.00	
506	Telephone & Telegraph	2,500.00	
507	Printing & Mimeographing	2,500.00	
509	Supplies	5,800.00	
511	Dues & Contributions	2,000.00	
512	Legal — non-legislative	$ 5,000.00	
513	Insurance	6,200.00	
514	Equipment Maintenance	1,810.00	
515	AMA Commission Expense	850.00	
516	Postage	3,500.00	
517	Miscellaneous	100.00	
518	Blue Cross/Blue Shield	2,000.00	
520	Contractual Services	100.00	
521	Audit	1,250.00	
522	General Overhead Recovery	(4,000.00)	
524	Furniture and Fixtures	—0—	
600	Depreciation Expense	1,200.00	
	TOTAL GENERAL FUND EXPENDITURES		$114,980.00
DIRECT COMMITTEE EXPENDITURES			
500a	Annual Meeting	$ 26,950.00	
500b	Articles of Incorporation	10.00	
500c	Benevolent & Loan Fund		
	Meeting Expense	50.00	
	Scholarship Grants	3,500.00	
500d	Board of Directors	1,500.00	
500f	Executive	300.00	
500h	Grievance	50.00	
500i	History and Obituaries	75.00	
500j	Industrial Relations	5.00	

500k Legislative		
Legal	9,000.00	
Other	300.00	
500l Medical Economics	300.00	
500p Professional	4,300.00	
500r Public Relations	15,000.00	
500s Publishing	44,875.00	
500t Scientific Assembly	200.00	
500u Woman's Auxiliary	1,000.00	
500v Resolution #6 (Abortions)	10.00	
500w Procurement and Assignment	10.00	
500y Governmental Services	5,000.00	
500z Resolution #15 (M.D.s on Hosp. Boards)	5.00	
TOTAL COMMITTEE EXPENDITURES		$112,440.00
TOTAL EXPENDITURES		227,420.00
CONTINGENCY FUND		$ 6,660.00

and be it further

RESOLVED, that the Annual Dues of the Arizona Medical Association, Inc. be continued at $100.00 for active members; and $5.00 for subscription to Arizona Medicine Journal; totaling $105.00.

ADOPTED APRIL 26, 1969

RESOLUTION NO. 2

Introduced by Maricopa County Medical Delegation.

Subject — County Membership on State Committee

WHEREAS, it is desirable to maintain liaison between comparable State and County Committees; therefore be it

RESOLVED, that the President of the Arizona Medical Association shall appoint to each State Committee the appropriate county committee chairman where feasible.

NOT ADOPTED, APRIL 26, 1969

RESOLUTION NO. 3

Introduced by Maricopa County Medical Society Delegation — February 28, 1969. Substitute Resolution by Reference Committee on Resolutions.

Subject — Anti-cigarette smoking.

WHEREAS, the American Medical Association has failed to take an active stand against cigarette smoking and cigarette advertising; and

WHEREAS, the physician must play a leading role in preventive medicine; therefore be it

RESOLVED, that the Arizona Medical Association urges the House of Delegates of the American Medical Association to actively participate in an anti-smoking campaign; and be it further

RESOLVED, that this resolution shall be presented and supported by our Delegates to the next meeting of the House of Delegates of the American Medical Association for their consideration.

SUBSTITUTE RESOLUTION ADOPTED, APRIL 26, 1969

RESOLUTION NO. 4

Introduced by Board of Directors, The Arizona Medical Association.

Subject — Allocation of Interest Accrued in Connection with the Building Program Retroactive to the Establishment of the Building Fund.

WHEREAS, Resolution No. 14, adopted in 1964, committed the interest earned on savings accounts to be credited to the Scholarship Fund; and

WHEREAS, the Building Fund was not then an existing account; and

WHEREAS, the Association must use every available financial resource in meeting the present building commitments; therefore be it

RESOLVED, that this House of Delegates go on record specifically exempting the interest earned by the Building Fund, and that this interest be applied to the present building program, retroactive to the establishment of the Building Fund.

ADOPTED, APRIL 26, 1969

RESOLUTION NO. 5

Introduced by Board of Directors, The Arizona Medical Association, Inc.

Subject — Removal of Drugs from the market on the basis of NAS/NRC Panel Reports.

WHEREAS,

1. the Food and Drug Administration (FDA) has recently published notices in the Federal Register of proposed action whereby certain drugs may be removed from the market which practicing physicians have used widely with beneficial results for a number of years; and
2. the proposed action is based upon the recommendations of panels of the National Academy of Sciences - National Research Council, Drug Efficacy Study Group (NAS/NRC) and apparently without the benefit of consultation with practicing physicians who have used the drugs; and
3. if there is to be a meaningful evaluation of these drugs in addition to considering the panel reports, the FDA also should make a thorough investigation to obtain pertinent data and opinions from the practicing physicians who have used the drugs; and
4. notices published in the Federal Register are not an adequate means for obtaining such data and opinions; now therefore be it

RESOLVED, that The Arizona Medical Association, Inc., disapproves the removal of the drugs referred to above from the market on the basis of NAS/NRC panel reports and without a thorough investigation by the FDA to obtain pertinent data and opinions from practicing physicians who have used the drugs; and be it further

RESOLVED, that the Food and Drug Administration is hereby requested to take appropriate action to institute a thorough investigation to obtain such data and opinions from pratcicing physicians who have used the drugs; and be it further

RESOLVED, that the representatives of the State of Arizona in the United States Congress are hereby requested to introduce appropriate legislation to amend the Federal Food, Drug and Cosmetic Act to insure that the Food and Drug Administration conducts such an investigation in similar circumstances before proceeding to remove a drug from the market; and be it further

RESOLVED, that the Secretary of The Arizona Medical Association, Inc., is hereby directed to send copies of this resolution to the Congressmen representing the State of Arizona in the United States Congress, requesting them to sponsor such legislation; and to the Federal Food and Drug Administration, requesting them to institute appropriate action to conduct a thorough investigation to obtain pertinent data and opinions from practicing physicians who have used the drugs referred to above; and be it further

RESOLVED, that the House of Delegates of The Arizona Medical Association, Inc., instruct its Delegates to The American Medical Association to introduce a similar resolution in the House of Delegates of that body at its annual meeting July next.

ADOPTED, APRIL 26, 1969

RESOLUTION NO. 6

Introduced by No. 6-69 Maricopa County Medical Society Delegation, March 24, 1969; No. 7-69 Ad Hoc Committee on Resolution No. 6, April 7, 1969; No. 8-69 Ad Hoc Committee on Resolution No. 6, April 7, 1969; No. 9-69 Ad Hoc Committee on Resolution No. 6, April 7, 1969; and No. 12-69 Arthur V. Dudley, Jr., M.D., President.

Subject — No. 6-69 New Revision of Therapeutic Abortion Law; No. 7-69 Abortion; No. 8-69 Abortion; No. 9-69 Abortion; and No. 12-69 Therapeutic Abortion.

WHEREAS, the Arizona Medical Association in its past two meetings of its House of Delegates has gone on record as favoring liberalization of the Arizona statute on therapeutic abortion; and

WHEREAS, the Arizona Medical Association has resolved to continue to encourage and favor such legislation; and

WHEREAS, a public opinion survey taken in Maricopa and Pima counties by Merrill Research of Tempe, Arizona, and released in February, 1969, revealed that two-thirds (67%) of the registered voters in these two most populous counties of the State are in favor of liberalizing the existing abortion law; therefore be it

RESOLVED, that the Arizona Medical Association goes on record as favoring new legislation and if necessary an initiative measure liberalizing the Arizona therapeutic abortion statute.

SUBSTITUTE RESOLUTION ADOPTED, APRIL 26, 1969

RESOLUTION NO. 10

Introduced by Arthur V. Dudley, Jr., M.D., President — April 8, 1969. Substitute Resolution by Harold W. Kohl, Jr., M.D., —Pima County Medical Society.

Subject — Continuing Education (Original Resolution), Substitute Resolution — Periodic Medical Relicensure.

WHEREAS, it has always been to the patient's best interest that physicians continue to add to their fund of medical knowledge; and

WHEREAS, most physicians conscientiously pursue courses of continuing education; and

WHEREAS, ArMA and the Arizona Regional Medical Program are developing a statewide program of continuing medical education; therefore be it

RESOLVED, that this House of Delegates instruct its legal counsel in consultation with the Board of Medical Examiners to investigate methods for effecting periodic relicensure; and be it further

RESOLVED, that the President of the Arizona Medical Association appoint a study committee to work with the Board of Medical Examiners to determine the mechanics of periodic relicensure and prepare a formal report to be considered at the next Annual Meeting of the House of Delegates.

SUBSTITUTE RESOLUTION ADOPTED, APRIL 26, 1969

RESOLUTION NO. 11

Introduced by Arthur V. Dudley, Jr., M.D., President.

Subject — American Medical Association Bylaws.

WHEREAS, the American Medical Association is undergoing an in-depth survey in respect to its function, organization and purpose, and

WHEREAS, the AMA is being criticized both from within and outside the parent organization as failing to reflect the attitudes and beliefs of its physician membership, and

WHEREAS, the present Bylaws of the AMA allow a Trustee to serve three 3 year terms without regard to age or infirmity, and

WHEREAS, the present survey recommends that Trustees serve two 4 year terms; therefore be it

RESOLVED, that the ArMA delegates to the AMA House of Delegates be instructed to support this concept of two four-year terms and to encourage the candidacy of new, qualified members of the AMA Board of Trustees and thus promote limitation of tenure based on active competition to these important offices.

ADOPTED, AS AMENDED, APRIL 26, 1969

RESOLUTION NO. 13

Introduced by Robert S. Keller, M.D.

Subject — ROTC Program.

WHEREAS, The members of The Arizona Medical Association, Inc., are a major group of responsible patriotic citizens, truly and deeply concerned with the future freedom of their country, the future good of its youth, and the preservation of its democratic institutions and, WHEREAS, The Arizona Medical Association recognizes that the prime objective of our existing educational institutions is not only to prepare our youth with technical excellence for self-supporting careers, but also, and most importantly, to instill the disciplined character and worthwhile principles that will build inspired leaders and sound citizens for the future and,

WHEREAS, The most neglected phase of medical health attention takes place during youth and adolescence. To advance the cause of greater mental and physical well-being in this prime group of potentially useful citizens, the Arizona Medical Association would undertake to provide professional medical manpower. The necessary annual physical examination, without additional cost to the harried taxpayer, would insure the efficiency of the physical fitness segment of the proposed R.O.T.C. system, as well as constituting a much needed check on our country's vital growing generation. As concerned citizens and taxpayers the Arizona Medical Association would, by endorsing these proposals, exhibit in a meaningful way its deep concern in a direct and logical means to aid our disrupted educational institutions regain their prime objectives and justify their expense to the taxpayer and,

WHEREAS, The benefits of a required R.O.T.C. Program would be (1) the substitution of a program of all inclusive meaningful disciplined activity for the present physical education program, which has failed signally in providing all-round physical fitness for the average student. It is well known that the prime goal of the present program has become the grooming of the athletically inclined to entertain the public; (2) the furtherance of realistic integration as all fit students, regardless of race, creed, color or socio-economic status would be required to take part; (3) a practical solution of the problems of campus disorders. The majority of average students are in school to learn, and at present have no organized voice against communist subversion and attack. Given the R.O.T.C. requirement, with patriotic leadership and the directed responsibility to protect their own peers and make unnecessary the use of outside police and security forces on campus; (4) required faculty cooperation with the R.O.T.C. program and objectives would help re-orient the teaching force in the direction of worthwhile useful student goals. Such patriotic leadership is sadly absent in some faculty segments today; and (5) student drug use and addiction would be contained, and finally controlled, when restored student goals and worthy faculty leadership result from cooperation with an effective R.O.T.C. program, therefore be it

RESOLVED, That The Arizona Medical Association, Inc., recommend for the consideration of Governor Williams and the Arizona State Legislature that an R.O.T.C. program shall be required for all male students in all tax supported educational institutions. A minimum of four hours of instruction and drill per week shall be required in the third and fourth years of high school. The performance of these students in their R.O.T.C. obligations shall constitute one criterion of character and patriotic fitness for education in a tax supported college. A minimum of six hours per week shall be required in all Junior and four year tax supported colleges. The quality of performance of college R.O.T.C. obligations shall determine the worth of the students continuing college education at the taxpayer's expense. R.O.T.C. as recommended shall replace fifty to one hundred percent of present physical requirements, and be it further

RESOLVED, that the support of this proposal be enlisted from other physical and mental health groups such as the Arizona State Dental Association, the Arizona Osteopathic Medical Association, the Arizona Hospital Association, the Arizona State Nurses' Association and all other Arizona professional health organizations.

NOT ADOPTED, APRIL 26, 1969

RESOLUTION NO. 14

Introduced by Richard O. Flynn, M.D., President.

Subject — Honorary Lifetime Membership — The Arizona Medical Association, Inc. — Robert Carpenter.

WHEREAS, Bob Carpenter has faithfully served this organization for the past twenty years and in addition, has discharged his duties and responsibilities above and beyond that required of him in his capacity as Executive Secretary; be it hereby

RESOLVED, that the House of Delegates of the Arizona Medical Association go on record as commending Bob Carpenter for his contributions to this Association and wish him well in his future endeavors; and be it further

RESOLVED, that Bob Carpenter be made an Honorary Lifetime Member of the Arizona Medical Association.

ADOPTED, APRIL 26, 1969

RESOLUTION NO. 15

Introduced by John S. Carlson, M.D. — Maricopa County Medical Society.

Subject — Commendation of Edward Sattenspiel, M.D., Chairman, Scientific Assembly Committee.

WHEREAS, Doctor Ed Sattenspiel of Maricopa County Medical Society, Chairman of the state Scientific Assembly Committee, has presented this Body with an outstanding scientific program; therefore be it

RESOLVED, that he be therefor commended for his fine services to this Association.

ADOPTED, APRIL 26, 1969

RESOLUTION A-1

Introduced by Article of Incorpation and Bylaws Committee.

Subject — Chapter VI — Board of Directors — Section 9. Executive Director Amendment.

RESOLVED, That Chapter VI — Board of Directors, Section 9. Executive Eecretary; Offices, be amended to read:

The Board may employ an Executive DIRECTOR, who need not be a physician, and such other assistants and employees as it may deem necessary to facilitate and carry out the work of the Association, and shall specify their salaries and terms of employment. The Executive DIRECTOR shall be under the direction of the Association Secretary, but shall have the supervision of all other employees and shall serve as office manager of the Association.

The Board shall also make provisions for appropriate offices, furniture, fixtures and supplies therefor for the Association, its Executive DIRECTOR, assistants, and employees.

Note: all fully capitalized words are new material.

ADOPTED, APRIL 26, 1969

RESOLUTION A-2, A-4

Introduced by Articles of Incorporation and Bylaws Committee.

Subject — Chapter II — Membership Section 3. Classes of Membership Amendment.

RESOLVED, That Chapter II — Membership. Section 3. Classes of Membership, be amended to read:

(C) Associate Members

Associate members may be elected by the Board, upon recommendation of the society of the county in which such members reside, from those doctors of medicine, who are licensed to practice medicine and surgery in Arizona, but are (1) disabled and unable to practice, (2) retired from active practice and not eligible for Fifty-Year Club membership, 3) active members who leave practice to undergo a further training period lasting six months or more, or for military service, (4) INTERNS AND RESIDENTS WHO ARE PARTICIPATING IN AN APPROVED INTERNSHIP OR RESIDENCY PROGRAM IN THE STATE OF ARIZONA.

Rights. Associate members shall have all the rights and privileges of active membership except the right to serve as a Delegate or to hold elective office. They shall not be required to pay Association dues AND NOT BE ENTITLED TO RECEIVE ANY PUBLICATION OF THE ARIZONA MEDICAL ASSOCIATION EXCEPT BY SUBSCRIPTION OR BY GIFT.

(D) Service Members

UPON RECOMMENDATION BY A COUNTY SOCIETY, THE BOARD MAY ELECT AS SERVICE MEMBERS REGULARLY COMMISSIONED MEDICAL OFFICERS AND COMMISSIONED MEDICAL OFFICERS OF THE RESERVE COMPONENT WHO HOLD THE DEGREE OF DOCTOR OF MEDICINE OR BACHELOR OF MEDICINE, ON EXTENDED ACTIVE DUTY WITH THE UNITED STATES ARMY, THE UNITED STATES NAVY, THE UNITED STATES AIR FORCE, THE UNITED STATES PUBLIC HEALTH SERVICE AND THE PERMANENT MEDICAL OFFICERS OF THE VETERANS ADMINISTRATION.

Rights. Service members shall have all the rights and privileges of active members except the right to serve as Delegates, or to hold elective office. They shall pay one-quarter the dues of active members.

(E) Affiliate Members

Allifiate members may be elected to this Association by the Board upon recommendation by county societies from (1) those doctors of medicine who are duly accredited in Mexico, or in foreign countries, engaged in medical missionary and similar educational and philanthropic work, (2) Arizona dentists who are members in good standing of their local and state societies, (3) pharmacists who are active members of their Arizona State Association, (4) teachers of medicine and allied sciences who are not eligible to other membership in this Association (5) former active members of this Association, who are now in practice in another state, and (6) retired physicians holding degree of Doctor of Medicine and residing in Arizona.

Rights. Affiliate members shall enjoy the privileges of attending the scientific meetings. They shall not have the right to serve as Delegates, or to hold elective office. They shall pay no dues AND NOT BE ENTITLED TO RECEIVE ANY PUBLICATION OF THE ARIZONA MEDICAL ASSOCIATION EXCEPT BY SUBSCRIPTION.

(F) Honorary Members

The House of Delegates may elect at any annual session as honory members of this Association, doctors of medicine or other persons of this, or a foreign country, who are distinguished for their services or who have risen to preeminence in the profession of medicine and surgery, provided the candidate for such membership is, or has been, a guest of the Association, or has performed a meritorious service to the Association.

Rights. Honorary members shall enjoy the privileges of attending all scientific sessions, but shall not have the right to serve as Delegates or to hold any elective or appointive office. They shall pay no dues AND NOT BE ENTITLED TO RECEIVE ANY PUBLICATION OF THE ARIZONA MEDICAL ASSOCIATION EXCEPT BY SUBSCRIPTION.

Note: all fully capitalized words are new material.

SUBSTITUTE RESOLUTION ADOPTED, APRIL 26, 1969

RESOLUTION A-3

Introduced by Articles of Incorporation and Bylaws Committee.

Subject — Chapter IX — Dues and Assessments, Section 6. Refunds.

RESOLVED, That Chapter IX — Dues and Assessments, Section 6, Refunds, be amended to read:

DUES AND ASSESSMENTS MAY BE REFUNDED AT THE DISCRETION OF THE BOARD OF DIRECTORS OF THE ARIZONA MEDICAL ASSOCIATION UPON RECOMMENDATION OF A COMPONENT COUNTY MEDICAL SOCIETY.

ADOPTED, AS AMENDED, APRIL 26, 1969

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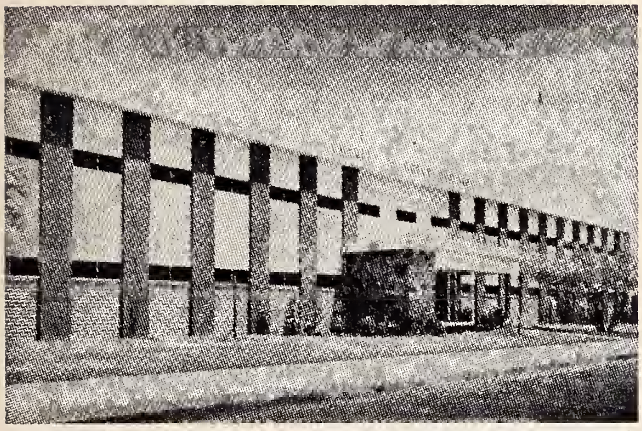

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  Sue Boyett, M.D.
DERMATOLOGY
  Ocie Carl Yarbrough, M.D.
EAR, NOSE and THROAT
  Richard Zonis, M.D.
FAMILY COUNSELING
  Leo Stein
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  Joseph Best, M.D.
  William B. McGahey, M.D.
  John A. Martin III, M.D.
GENERAL SURGERY
  Boyd H. Metcalf, M.D.
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INTERNAL MEDICINE
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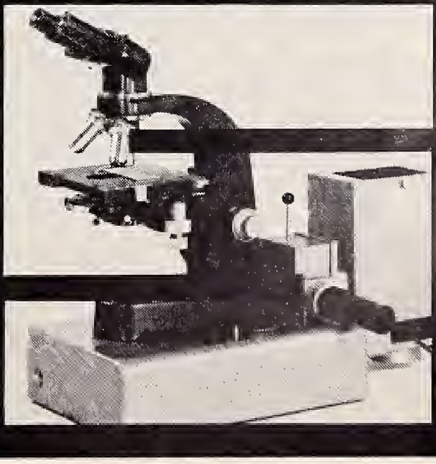

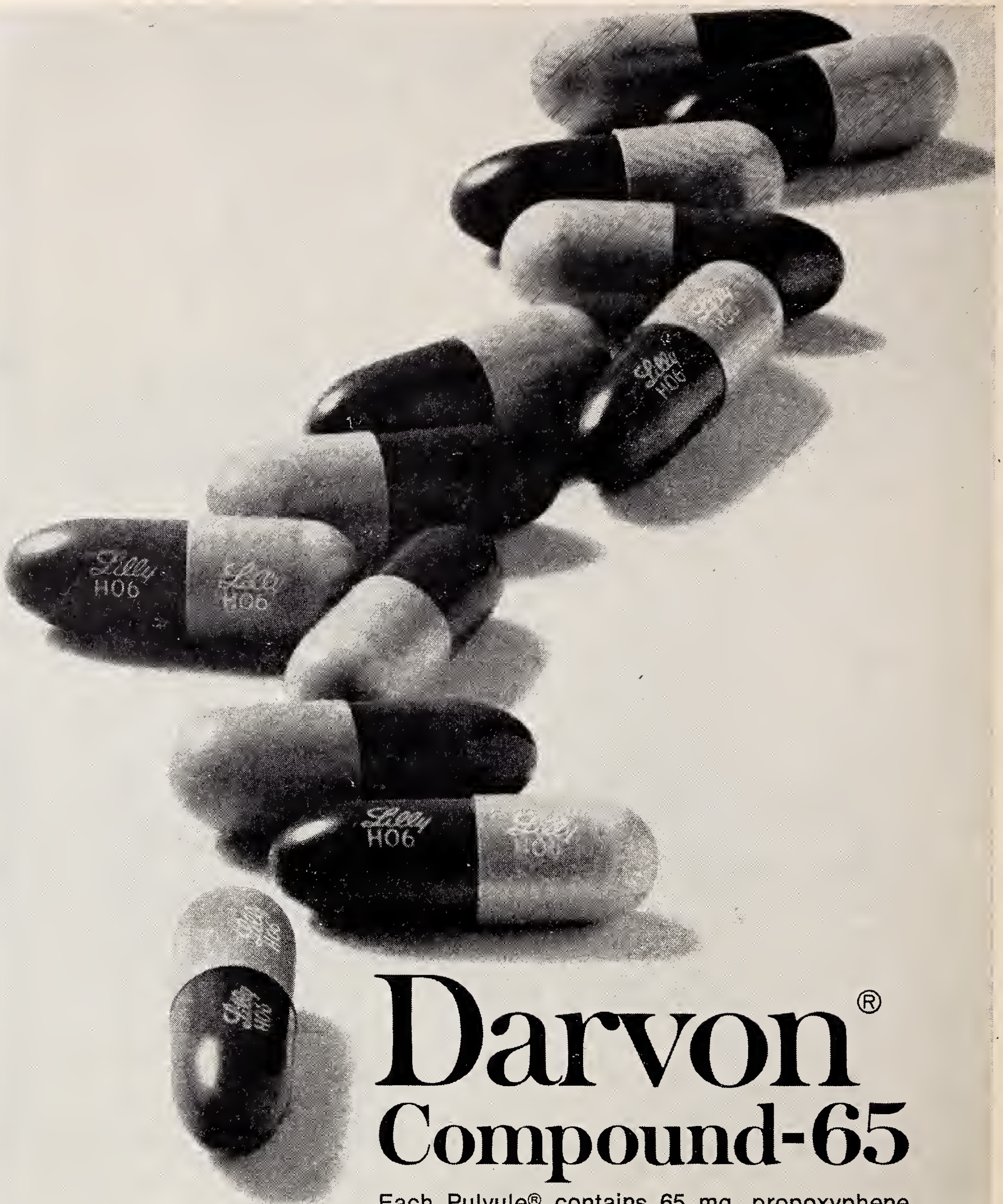

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Original Articles

DONALD R. MILES, M.D.

Computer analysis is becoming an important technique in medical practice. This article demonstrates how computers can be used in evaluating various aspects of eye muscle surgery.

POSTOPERATIVE RESULTS IN CHILDHOOD ESOTROPIA

To obtain a satisfactory cosmetic and functional result through surgical treatment of the child with strabismus requires the proper evaluation of sensory and motor factors by the ophthalmic surgeon. The etiologic factors of strabismus are complex and, when the rational treatment indicates the necessity for a corrective operation on the ocular muscles, the type and amount of muscle recession or resection becomes most important. Unfortunately, strabismus is of congenital or early postnatal onset and the afflicted child is unable to answer the many subjective tests required for precise analysis of the problem. Therefore, surgical intervention frequently is initiated and planned from the results of objective testing by the surgeon. The predicted correction from a specific amount of recession or resection of the ocular muscles is related to three general areas:

1. The theoretical mechanical effects mathematically determined
2. Preoperative sensory and motor status of the individual patient
3. The review and reappraisal of patients previously receiving similar surgical treatment.

It is the purpose of this report to evaluate clinically in a retrospective case-study manner two of the most common types of operation for the correction of the young child with esotropia — the symmetrical bimedial recession of the medial rectus muscles and the asymmetrical recession of the medial rectus muscle and resection of the lateral rectus muscle on the same eye.

Materials and Methods

A digital computer was utilized to aid in the evaluation and compilation of the various aspects of information from each case, and the information was programmed on IBM cards correlated with a questionnaire form filled out on each case.

The source material was obtained from the University of Iowa Hospital Department of Ophthalmology Strabismus Clinic from the period of January 1, 1950, to January 1, 1965. All cases included in the study had at least a six-month follow-up, involved children below ten years of age at the time of the operation, and had either a bimedial recession operation or a recession-resection operation as the initial surgical procedure. Since the bimedial recession procedure was performed less often during this 15-year period, this was the first group sorted from the files. A total of 145 bimedial recession operations was obtained, and an equal number of recession-resection operations was selected from the files in a comparable chronological pattern over the 15-year span. A paper describing postoperative differences between the two groups has been reported previously.[1]

In this report three areas are evaluated using the entire 290 cases as one general group:

1. The average amount of correction obtained correlated to the amount of recession or resection performed on the rectus muscles
2. The influence of the size of the preoperative esotropic deviation on the amount of correction obtained
3. The change of the sensory status from preoperative to postoperative period in relation to under- or overcorrection of the esotropia.

Results

Table I categorizes the entire group. In the bimedial recession operation both medial rectus muscles were recessed equally; the range was from 2 - 5 mm, with the 3 mm and 4 mm groups containing the bulk of the cases. In the recession-resection operations the classification was slightly different with four groups arranged so that the main division was the amount of recession performed on the medial rectus — 3 mm or less and 4 mm or more. Then the two groups were divided into four by separating those in which the lateral rectus resection equaled more than twice the amount of the medial rectus recession from the ones that equaled less than twice the amount of the recession. In this way, a determination in each operation could be made of the relative emphasis of the recession of the medial rectus versus the resection of the lateral rectus.

TABLE I
CLASSIFICATION OF OPERATIVE GROUPS

Bimedial Recession		No. of Patients
2 mm		1
3 mm		46
4 mm		91
5 mm		7
Recession—Resection		
Medial Rectus	Lateral Rectus	
3 mm or less	6 mm or less	27
3 mm or less	7 mm or more	11
4 mm or more	7 mm or less	49
4 mm or more	8 mm or more	58

Table II presents the measurements of the amount of correction obtained by the operation. The bimedial recession operation resulted in an orderly increase in the amount of correction obtained correlated with the amount of operation performed. One interesting aspect was the large jump in the amount of correction occurring with the 5 mm bimedial recession — the average increased by approximately 20 prism diopters over the 4 mm group. This would seem to indicate that, when a certain limit is reached in the weakening of the medial rectus by recessing it, perhaps either the mechanical or the physiological function of the muscle is so affected that a large amount of change can be expected with the next millimeter of recession performed on the muscle.

The asymmetrical recession-resection part of Table II shows little change when a relatively small recession of the medial rectus was performed whether the lateral rectus had more or less resection. In fact, the averages for the first two groups are somewhat paradoxical since the group which had more emphasis on the lateral rectus resection showed less of a corrective change. However, when the amount of the resection becomes relatively larger, as is seen in the last two groups with a 4 mm recession of the medial rectus, the effect becomes evident and shows a definite increase when a larger amount is resected from the lateral rectus. The implication would be that the effect of resection of the lateral rectus becomes additive to the medial recession only when the resection is of a larger amount.

TABLE II
AVERAGE AMOUNT OF CORRECTION
Measured in Prism Diopters at Near

Bimedial Recession	
2 mm	8.00
3 mm	17.61
4 mm	25.98
5 mm	45.14
Recession—Resection	
3 mm/6 mm	21.81
3 mm/7 mm	19.91
4 mm/7 mm	28.57
4 mm/8 mm	35.45

In Table III another computerized analysis shows the four largest surgical groups further divided into groups having either a large or a small preoperative deviation. The dividing line between the large and small groups was set at 35 prism diopters of preoperative esotropia measured at near. The amount of correction obtained was compared with the amount of preoperative esotropia in each of the groups. It is interesting to note the consistent pattern in each group in which the amount of correction obtained is al-

TABLE III
PREOPERATIVE DEVIATIONS
Measured in Diopters at Near

Bimedial Recession	3 mm	(46)	4 mm	(91)
Large	25.06	(16)	38.86	(59)
Small	17.60	(30)	16.75	(32)
Recession-Resection	4 mm/7 mm	(49)	4 mm/8 mm	(58)
Large	31.40	(30)	40.33	(52)
Small	19.26	(19)	16.83	(6)

ways considerably less when the amount of esotropia existing before the operation is small.

In Table IV a study was made of the sensory changes that were reported in patients having abnormal retinal correspondence preoperatively. Following the operation each patient was classified according to whether there was a residual of esotropia (an undercorrection) or a secondary exotropia (an overcorrection). Although the total number of patients with a residual of esotropia was approximately six times the number of patients with a postoperative exotropia (the exact numbers being 61 and 11), the change to normal retinal correspondence was significantly different between the residual esotropes and the secondary exotropes with the percentage obtaining normal retinal correspondence being much higher in the overcorrected patients.

TABLE IV
SENSORY STATUS CHANGE FROM PREOPERATIVE ARC TO POSTOPERATIVE NRC

Postoperative Esotropia	
Bimedial Recession	50%
Recession-Resection	54%
Postoperative Exotropia	
Bimedial Recession	78%
Recession-Resection	100%

Discussion

Although retrospective studies of the type just presented have their limited value, much can be gained from the cataloguing of such information. As time passes and more sophisticated means of charting and evaluating patients are achieved through computerized methods, certain trends and factors will become evident that probably would be hidden to the individual practitioner whose scope of reference would be limited to those patients he has cared for personally.

From this study there is an indication that when the surgeon recesses each medial rectus more than 5 mm the amount of correction obtained increases greatly and that this may be due to changing the muscles' ability to react normally. Also, the finding that the lateral rectus muscle must be resected a goodly amount before an additive corrective effect can be expected brings up an interesting question: Is the resulting effect brought about by the strengthening of the muscle's action, or is the surgeon creating an anchoring effect of the lateral rectus to the globe whereby the muscle cannot lengthen and thus mechanically limit the adduction of the eye? As Burian[2] has previously advocated, multiple surgical operations for a more balanced correction of ocular motor abnormalities is preferred to an attempt to correct the entire deviation with an operation which will cripple certain muscles to the point that they may create incomitant and secondary imbalances. Furthermore, the comparison of large and small preoperative deviations suggests the wisdom of a moderate approach to the amount of recession or resection performed on the extraocular muscles. As shown in Table IV, the resulting correction in a large preoperative deviation may be more than the surgeon expected; thus, a conservative approach may yield much better results than a large recession or resection on the rectus muscles.

It was noteworthy that, when abnormal retinal correspondence was present preoperatively, a significantly higher percentage returned to normal retinal correspondence when a secondary exotropia occurred postoperatively. Although this change is small consolation to the patient with a postoperative exotropia, the return to normal correspondence may bring about a more stable final result after a second surgical procedure for correction of the exotropia. This finding would tend to confirm the importance of the physiological scotoma existing in the nonfixating eye.[3] Since the exotropia would bring a section of the retina outside the physiological scotomatous area into relationship with the other eye, the preoperative sensory adaptation of abnormal retinal correspondence would no longer serve the purpose of avoiding a confusion of visual images between the eyes and thus would tend to disappear. The above finding would tend to give some basis to attempts to stimulate the nonfixating eye with reverse prisms and calibrated occlusion as described by Rubin[4] and to the esotropic convergence response in relation to exotropia reported by Hardesty.[5]

Presented at the Seventy-Seventh Annual Meeting of the Arizone Medical Association, April 23-27, 1968, Phoenix.

From the Department of Ophthalmology and Neurosensory Center, College of Medicine, University of Iowa, Iowa City, supported by Program Grant No. B-3343, National Institute of Health, Bethesda, Maryland.

Acknowledgment: The guidance of Dr. Hermann Burian of the Department of Ophthalmology, College of Medicine, University of Iowa, and the assistance of Mr. John Krall and Dr. Paul Leaverton of the Department of Preventive Medicine and Environmental health, College of Medicine, University of Iowa, in programming the computer material for this paper is greatly appreciated.

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DISSEMINATED VISCERAL PRIMARY CANDIDIASIS

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An unusual well documented case of disseminated Candidiasis is presented. The factors predisposing to such infections are discussed.

Disseminated visceral candidiasis, as a clinical entity causing primary tissue lesions, is not common. Since the demonstration of Candida albicans as an etiological factor in a patient with thrush by Langenbeck in 1839, and the description of the organism by Robin in 1843, the medical literature on candidiasis has been voluminous.

However, the overwhelming majority of papers refer to cutaneous or mucocutaneous disseminations and have been, therefore, of interest mainly to dermatologists and dermatopathologists. Observations of visceral dissemination are considered, most of the time, to be secondary infections in patients with other serious and debilitating primary conditions.

The concept that Candida can be considered as an endogenous organism, because it can be carried by the normal individual, apparently in the same manner as staphylococci, pneumococci and meningococci, is well accepted. Not only saprophytic, but also pathogenic strains have been isolated from the mouth, vagina and intestinal tract.[1] Secondary invasion by saprophytic and "opportunistic" yeast-like fungi is a rather frequent occurrence, particularly in patients with a prolonged antibiotic therapy.[2]

It follows that the presence of Candida in the blood, or in the tissues is not always sufficient evidence of its pathogenicity, and in some cases the cause of the condition is difficult to ascertain.[3]

Proof of a direct cause-effect relationship must be found then, if we are to accept a Candida visceral dissemination as producing per se, serious disease or even death as a direct consequence of its virulence. A few conditions appear to be necessary: a) presence of the organism in the tissues, blood and/or other body fluids. Simultaneous presence of bacteria requires critical analysis of their possible role in the condition; b) since the mere finding of the organism is not criterion enough, there should be lesions which represent the reaction of the body to the infection. The most frequent is inflammation, involving organs other than the skin or superficial mucosas; c) the autopsy — the condition is characterized by a very heavy mortality — should show anatomicopathological findings consistent with an infection present "for some time" before death. The requirement "for some time," though apparently vague, is necessary to rule-out terminal or agonal invasions by the fungus, which, obviously due to lack of time, cannot produce tissue reaction such as abscesses, or even less likely, granulomatous lesions; d) the presence of conditions whereby the pathogenicity of Candida is provoked or enhanced, such as chronic debilitating diseases, obesity, advanced age and particularly, diabetes and prolonged antibioltic treatment.

The following case of a fatal visceral disseminated candidiasis fulfills the above conditions and will illustrate some clinical and pathological aspects.

Case Report

A 64-year-old woman was admitted to Maricopa County General Hospital in December, 1964 with a clinical picture of septic shock attributed to a perforated diverticulum of the sigmoid colon.

The past history revealed that she underwent cholecystectomy and appendectomy at age 23, and more recently had asthma and chronic bronchitis, in addition to a questionable heart attack.

She was treated intensively with neomycin and sulfasuxidine and given blood transfusions before a right transverse colostomy was done. The post-operative period was complicated by pneumonitis and urinary infection, but she eventually recovered and was discharged. A few months later, during clinical evaluation and work-up for definitive surgery, a glucose tolerance test showed a diabetic curve.

In October, 1965, she was readmitted and a left hemicolectomy was considered. At this time the physical examination revealed an alert, cooperative, somewhat dehydrated patient, with normal vital signs. The lungs had coarse rales and expiratory wheezes, and the abdomen showed a well-functioning colostomy. The CBC showed 11.9 gm. of Hb. per 100 cc. of blood, a Hct. of 41 volumes% and 7,400 WBCs. For eight days the patient was prepared with neomycin, sulfasuxidine and enemas. At surgery, sigmoid diverticulitis with marked fibrosis was found, and a left hemicolectomy with low anterior anastomosis and closure of the colostomy was performed.

The post-operative period was again complicated by atelectasis and pneumonitis. Marked abdominal distention developed, an abscess formed in the abdominal wall, with a large amount of foul-smelling, purulent material, which yielded E. coli, group A beta streptococci and pseudomonas. She was intensively treated with Chloromycetin, Coly-mycin, fluids, blood and nasogastric suction. The abdominal distention increased and no bowel sounds were detected. The electrolytes showed metabolic acidosis and the blood sugar was 212 mg. per 100 cc. of blood.

She continued in a down-hill course, and expired on the 13th post-operative day. A blood culture, taken shortly before death, revealed "yeast forms" after 24 hours and no other bacterial growth.

Autopsy Findings

Gross Examination: The abdomen showed a mid-line, necrotic and suppurating surgical incision. The thorax showed the pericardial cavity obliterated by fibrous adhesions, and a moderate amount of clear yellow fluid in each pleural space. About 300 ml. of foul seropurulent-sanguineous fluid were found in the peritoneal cavity. The thyroid gland was normal in size and shape, but the cut sections showed small, gray-yellow nodules scattered in the parenchyma. The lungs were heavy, with increased consistency and large amounts of frothy fluid. The heart was enlarged (480 gm.), rather soft in consistency, and there was advanced coronary arteriosclerosis. The liver weighed 2820 gm., with a markedly increased consistency, and the cut surfaces had a dark brownish color, as well as marked fibrosis. The esophagus, stomach and small intestine were unremarkable, except for a small prepyloric ulcer. There was absence of most of the left colon, with a well-functioning, intact anastomosis between the right transverse colon and the rectum. The kidneys showed a dull gray external surface, studded with small yellow-gray nodules. Cortical hemorrhages and abscess formation at the papillae were also seen. The pancreas and adrenals were grossly normal. The rest of the autopsy was unremarkable.

Microscopic Examination: The thyroid (Figure 1) showed interstitial abscesses centrally occupied by masses of Candida organisms, showing both the yeast and the mycelial phase. The filaments were surrounded by leukocytes and occasionally went through vessel walls. The lungs showed only bronchopneumonia and edema; no fungi were seen. Sections through the myocardium showed large numbers of small abscesses (Figure 2), consisting of necrotic muscle fibers, C. albicans organisms and leukocytes. No organisms were seen in the endocardium. No fungi were found in the liver, spleen or pancreas, but those organs showed large amounts of hemosiderin. In the liver, the pigment was deposited not only in the Kupffer's cells but also in the liver cells, and there was marked cirrhosis of the portal type. The esophageal mucosa was extensively invaded by mycelial elements, and the same changes were noted in the intestinal mucosa. The kidneys revealed marked acute interstitial inflammatory changes, with formation of small intertubular abscesses containing mycelia and yeast-like elements (Figure 3). Marked inflammation and necrosis of the papilla were also noted. Extensive areas of skeletal muscle, main-

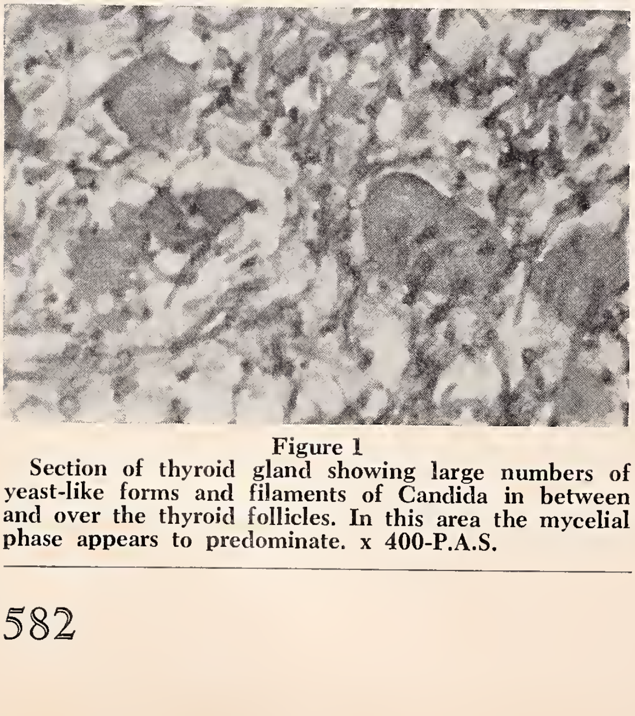

Figure 1
Section of thyroid gland showing large numbers of yeast-like forms and filaments of Candida in between and over the thyroid follicles. In this area the mycelial phase appears to predominate. x 400-P.A.S.

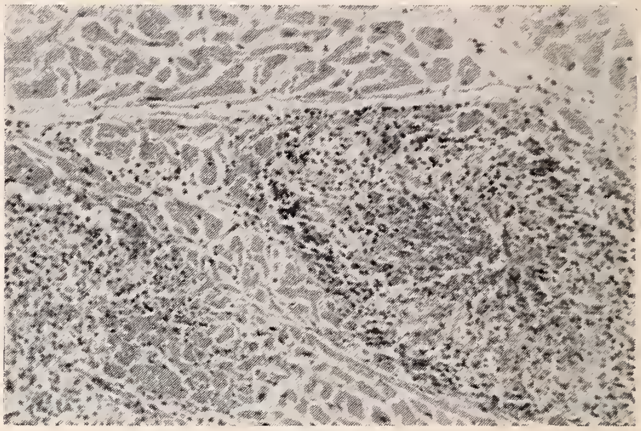

Figure 2
Section of myocardium at low magnification, showing part of two abscesses containing a large number of organisms, mostly one-celled, intermixed with leukocytes and necrotic muscle fibers. x 100 — H. and E.

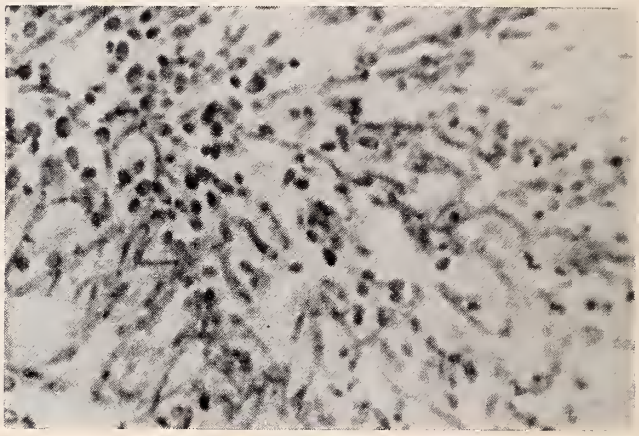

Figure 3
Section of kidney at the level of the medulla, showing a large number of mycelial forms and a few yeast-like organisms. x 400 — P.A.S.

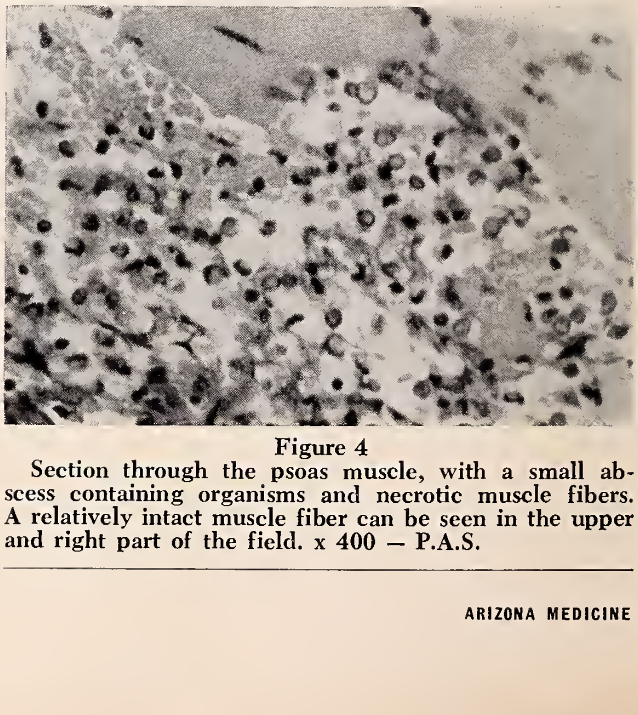

Figure 4
Section through the psoas muscle, with a small abscess containing organisms and necrotic muscle fibers. A relatively intact muscle fiber can be seen in the upper and right part of the field. x 400 — P.A.S.

ly in the abdominal wall, psoas and diaphragm showed acute myositis with small Candida abscesses. In the skeletal muscle the organism was represented mainly by one-celled elements with very few filaments.

Discussion

Our patient died with an overwhelming Candida infection, with visceral manifestations and a background which repeats the conditions classically considered essential for the development of this serious event.

The presence of diabetes in these patients has been mentioned repeatedly. So strong is this concept, that some believe that any patient with candidiasis should be considered potentially diabetic; and that the infection may be the first manifestation of diabetes.[4] However, it is interesting to note that in the excellent review of 29 cases by Louria et al,[5] only 2 patients had diabetes.

The presence of a protracted, debilitating illness hangs heavily in the background of these patients, and our case is no exception. Surgical maneuvers with opening of the intestinal lumen should also be mentioned.

Observations on the effect of antibiotics have also been numerous. Our case has a similiar situation. Explanations for this fact are many. Some observers believe not only in disappearance of competition from bacteria, but also in a direct growth-stimulating effect of the antibiotic on Candida.[2]

The origin of the fungemia is, in the great majority of cases, endogenous. However, there can be external contamination. Injections may introduce the organism into the deep tissues or the blood stream. In these cases, endocarditis and perhaps meningitis appear to be some of the first localizations.[4, 6].

From the anatomic point of view, the main visceral localizations in our case were the heart, kidneys, thyroid, skeletal muscles and esophagus. Candida abscesses in the thyroid are rare. They are mentioned by Louria et al,[5] and Braude and Rock.[7] The kidneys appear to be the most frequently involved organ in systemic moniliasis, and the esophagus the most commonly affected segment of the alimentary tract.

We were unable to find cases with Candida lesions in the skeletal muscles, an outstanding feature in our case. The presence of hemochromatosis and liver cirrhosis does not appear to have any direct relationship with the condition, though it is interesting to note that of the 29 cases reviewed by Louria, 4 had cirrhosis.

Since cases of visceral disseminated candidiasis appear to be on the rise, and since they carry a high mortality, an effort should be made to discover this entity, from the clinical standpoint of view a task which may be very difficult indeed since there are no specific signs or symptoms.

According to Braude, the condition may be suspected clinically by two outstanding features; a) a background of prolonged antibiotic treatment in a protracted debilitating illness, and b) an abrupt decline in the clinical course with the development of fever, shock and depressed sensorium.

Demonstration of the organism in the blood — candidemia — is, of course, of real help in the diagnosis. Recently, evaluation of increased serum antibody titers to Candida with immunofluorescent technique, appears to offer an important diagnostic tool.[8]

Diagnostic problems continue even at autopsy. The condition may be overlooked, as there are no specific lesions to identify, and the organism is difficult to see in ordinary H. and E. sections if one is not looking for them.[9] Both Giemsa and P.A.S. stain the organism clearly.

Summary

Several points on the etiopathogenesis of Candidiasis are discussed with comments on diagnostic problems, contributory conditions and anatomic findings.

The discussion emphasizes the occurrence of "primary" visceral candidiasis, as a morbid entity per se, and the criteria to be fulfilled.

A case is presented with some unusual tissue involvement, including thyroid and strikingly, skeletal muscles.

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President's Page

PERIODIC RELICENSURE??

One of the more interesting resolutions passed at the recent state meeting was entitled "Periodic Medical Relicensure," or Resolution No. 10.

> WHEREAS, it has always been to the patient's best interest that physicians continue to add to their fund of medical knowledge; and
>
> WHEREAS, most physicians conscientiously pursue courses of continuing education; and
>
> WHEREAS, ArMA and the Arizona Regional Medical Program are developing a statewide program of continuing medical education; therefore be it
>
> RESOLVED, that this House of Delegates instruct its legal counsel in consultation with the Board of Medical Examiners to investigate methods for effecting periodic relicensure; and be it further
>
> RESOLVED, that the President of the Arizona Medical Association appoint a study committee to work with the Board of Medical Examiners to determine the mechanics of periodic relicensure and prepare a formal report to be considered at the next Annual Meeting of the House of Delegates.

The Board of Medical Examiners has already started to consider some method of periodic relicensure and this gives impetus to the Association coming up with their own ideas.

The problem was that no one had any good method of determining competency. The method used by the Academy of General Practice the last fifteen years, and now being used in Oregon, is one of counting hours of postgraduate education. The House of Delegates felt that there are many doctors who are able to keep up by reading, listening to tapes, joining journal clubs, going to hospital meetings, and don't need formal programs. Other doctors have been known to sign in for formal programs and promptly head for the golf course where they busily count hours.

The committee formed by the last resolve of Resolution No. 10 includes Doctors Boyden L. Crouch, Arthur V. Dudley, Jr., Clifford J. Harris, Paul B. Jarrett, Jack M. Layton, Chairman, and Melvin W. Phillips. It has the simple problem of recommending to the House of Delegates the methods of determining competency, how soon after graduation such competency should be determined, how often subsequently, and, perhaps more fundamentally, if relicensure is necessary at all. (I'm not sure I could stand doctors being much smarter than they are now!)

This concept is one that, if implemented, would involve all of us. Whereas you and I would have no trouble passing any quiz that might be proposed to keep our license to practice, I worry a little about the rest of the Association.

This committee needs all the help and ideas they can get. If you have any suggestions pro or con, send them to the Central Office or catch a member of the committee in the hall and help them out. To paraphrase the voting adage, if you don't have anything to say before the rules are made, don't complain after they are put into effect. . . .

Richard O. Flynn, M.D.
President

Dean's Page

REGIONAL MEDICAL PROGRAMS AND COMPREHENSIVE HEALTH PLANNING

PART II

There is another aspect to Comprehensive Health Planning that has not been covered in the description, thus far, of the relationship between it and Regional Medical Programs for Cancer, Heart Disease and Stroke. Briefly, the designated State agency for Comprehensive Health Planning which, in Arizona, is the Arizona Health Planning Authority, is charged with the responsibility for preparing a "state plan" relative to all Health Planning. The state plan is not a blueprint; rather, it is a statement which attempts to identify problems which impinge on the health of the citizens of our own state and a program of alternative routes for solving these problems.

Below the state level, especially around metropolitan areas, another organization now comes into play. This is called the Area-Wide Health Planning Council. In Arizona, at least two such Councils are now established and operating. In both instances, (and this is true elsewhere in the United States) these Councils are outgrowths, or expanded versions, of what were formerly hospital planning councils concerned only with facilities. Such limited objectives as this are inadequate to serve the purposes of Area-Wide Health Planning and, therefore, these Councils expanded themselves and assumed the larger responsibility for all planning that relates to health.

The system should work as follows. Locally, Area-Wide Health Planning Councils will do their own surveying relative to existing health problems. Then, having recognized the existence of these problems they will assess the facilities and resources that are available to tackle the problems. Last, they will propose routes and means by which deficiencies in facilities or resources can be made up and the problems resolved. All of these determinations would be done by the residents and health professionals of the individual towns and cities involved. The conclusion reached by the Area-Wide Health Planning Councils will then be forwarded to the Arizona Health Planning Authority where they will be combined with others from local areas into an overall state plan. Once adopted, this plan must also be approved by the Governor's office.

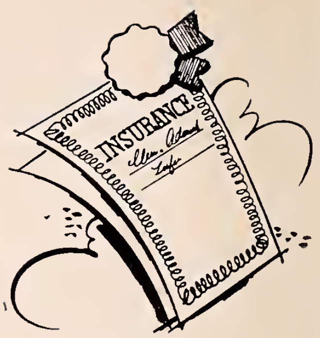
The plan will serve as an instrument against which all local applications for help will be measured. Since this hasn't been put to the test yet, one can only guess as to the way it will work but it seems likely that the procedure will be somewhat as follows. The Area-Wide Health Planning Council, having acknowledged the existence of a particular health problem, will stimulate appropriate local agencies, professional people, hospitals, etc., to advance a proposal for solving it. After the proposal takes shape, the cost of putting it into effect will be estimated and a budget attached. The proposal will be forwarded to the U. S. Public Health Service for funding, after having indicated that the proposal is consistent with the overall state plan. The application itself will then compete with other applications for the available funds through a priority system which is yet to be designed but which will almost certainly depend, to a great extent, on the degree of consistency that exists between the proposal and the state plan.

In Arizona, the beauty of this arrangement is that funds coming into the state for purposes of Regional Medical Programs and Comprehensive Health Planning will ordinarily not be competitive because the same general group of persons will be making judgments about the wisest use for these funds. To many of us, this makes a great deal more sense than having each institution and agency openly compete for the same funds without regard to duplication of effort, resources or facilities.

For many years now, a number of us have pleaded for the opportunity to be allowed to decide what problems are the most important in our area, and what steps we would like to take to eliminate them. Before we get too critical of the Comprehensive Health Planning Law we'd better realize that it is providing us with the vehicle we have asked for.

Monte DuVal

Editorial



WHERE WILL IT END?

Paul B. Jarrett, M.D.

In Michigan, an appellate tribunal reversed a lower court which prohibited the plaintiff from using the defendant doctor as an expert witness *against* himself. The court said that, "a civil defendant has no protection against subjecting himself to liability. If his testimony will provide facts which will aid the court in arriving at a just decision, he has the duty to testify. Any loss to the sporting aspect of the adversary proceedings would be outweighed by the benefit to the judicial system." The courts therefore make quite a distinction between a murderer or rapist and a physician on trial for malpractice. The criminal is prohibited from testifying against himself.

The time-worn and flimsy excuse for liberalizing rules of evidence and new methods for proving malpractice is the "conspiracy of silence." This seems to mean that if a physician reviews the evidence and doesn't find a departure from the standard of care and cannot therefore testify that malpractice existed, he is a "conspirator" against the patient who is praying for an award. It simply is not true that every law suit against a doctor resulted from malpractice. If a physician has done nothing wrong, why should the plaintiff's attorneys become so irate because other physicians refuse to testify that he has?

There has been no dearth of suits against doctors in recent years, and every case has produced physicians who testified in behalf of the plaintiff. Where is the conspiracy of silence?

The "locality rule" has virtually been eliminated by the courts. In the past, the plaintiff had to establish that the defendant physician departed from the standard of practice in the community in which the doctor practiced. The theory now imposed is that because of modern transportation, communication, text books, T.V. medical education, postgraduate courses, medical literature and meetings, even the "similar community" ruling is a thing of the past. A small

community without a resident radiologist, a pathologist who visits twice a week, no intensive care unit, no anesthesiologist, (perhaps a colleague who does the best he can in anesthesia in emergencies), no coronary care unit, no respiratory care unit, no interns or residents, no facilities for blood gases, no cardiologist, internist, pediatrician, allergist and so on, certainly does not give the small town doctor the same resources or ability to handle difficult and serious cases. It isn't the "wives" who are driving the doctors out of the small towns. It is the courts who hold the county practitioner now to the same standard of excellence as the physicians in the large centers with unlimited consultive and other facilities.

This and the doctrine of res ipsa loquitur, uninformed consent, recovery for mental suffering, the statute of limitations running from the time of discovery and some more permissive rulings, are in the opinion of many, as ridiculous as the recent ruling that unions have a vested interest in limiting production and it is therefore proper to fine union members for exceeding their quota.

Many professional liability carriers have withdrawn from the malpractice field. Some insurance companies will not write policies covering physicians who do any operative procedures, as a recent medical magazine article pointed out, a doctor makes thousands of life and death decisions in the course of his professional lifetime, yet if he makes one wrong decision, he may lose all he has worked a lifetime to acquire plus his professional reputation, and be unable to obtain liability insurance thereafter.

The physician shortage becomes more and more acute. Even so there is talk of re-licensing examinations at three year intervals and the training of sub-doctors. Who will accept the legal responsibility for these physician-aides? Certainly the number of M.D.s will be reduced by re-licensing, and early retirement because of the inability to obtain malpractice insurance or excessive premiums. Many excellent surgical assistants are not helping on cases they do not originate because this puts them in the category four classification of a surgical specialist with current premiums of $1280.00 per year, and no end to the premium rise in sight.

I have heard, but have not confirmed the statement that plastic surgeons in Florida cannot obtain malpractice insurance at any price. Some physicians who have had claims against them are rated up to above $4000.00 a year in premiums, and you are familiar with the mass concellations of malpractice policies in Utah and Alaska. Midwest Mutual cancelled all of their policy holders as of February 23rd. Aetna is no longer writing surgical specialists, and there is no doubt whatsoever about the courts practicing medicine. The high cost of medical care is greatly contributed to by the need for the physician to protect himself. It is questionable whether this makes for a higher standard of practice.

In Canada and Britain it is both unethical and illegal for a lawyer to accept a case on a contingency basis, and they have very few "nuisance" suits. Forty percent of a recent award for $1,500,000.00 is a pretty hefty fee for a few weeks work. What do you get for saving a life? What became of making the plaintiff pay court costs if he loses a suit? Recently a malpractice action in Flagstaff took five weeks in trial. What did this cost the taxpayers? How much important business was delayed as a result of the interminable presentation of the plaintiff's lawyer in a case that in many opinions should never have been permitted to come to court?

Will the day come when a doctor will be forced to say, "I'd like to help you, but I just can't take the risk!"

Where will it all end?

WORKMEN'S COMPENSATION GUIDE FOR PHYSICIANS

a continuing series

INDUSTRIAL COMMISSION OF ARIZONA

There are two public agencies concerned with administering claims under the Arizona Workmen's Compensation Laws, the principal one being The Industrial Commission of Arizona composed of five members appointed by the Governor with the consent of the State Senate for staggered terms of five years each. Duties of concern to the medical profession include administration of most labor laws and safety standards in industry, regulation of self-insured employers, processing of occupational disease claims, processing of claims against uninsured employers, notification of employers and insurance carriers of the filing of industrial claims, adjudication of all contested claims, processing of reopening petitions, determination of loss of earning capacity, commutation of awards to lump sums, fixing a schedule of physicians' fees, determination of the propriety of faith healing in industrial claims, investigation of claims processing by insurance carriers, and administration of a special fund to promote vocational rehabilitation of persons disabled in industry and to adjust second-injury liability and apportion losses between insurance carriers under the second-injury provisions of the law.

The expenses of the Commission are paid from an administrative fund created by 2% tax on all workmen's compensation insurance premiums paid to all carriers including self-insurers, self-raters, and the State Compensation Fund, but such fund is subject to legislative appropriation. The Special Fund referred to above is created by an additional 2% tax on all premiums paid to all carriers.

MANY RECENT INQUIRIES MAKE IT OBVIOUS THAT MANY PHYSICIANS DO NOT UNDERSTAND THE ORGANIZATIONAL AND STATUTORY CHANGES RESULTING FROM THE 1968 SPECIAL SESSIONS OF THE STATE LEGISLATURE.

Although very much over-simplified we include with this article two diagrams which demonstrate the lines of reporting of industrial injuries by all parties in most cases, before and after the effective date of the amendments to the law. These demonstrate only the initial reporting, except for the need that the physician direct subsequent reports and billings to insurance carriers. The broken lines demonstrate reporting which was not consistently done or was not mandatory. The solid lines show the reports required by statute. After acceptance of a claim which is uncontested, the principal lines of communication for the physician, other than with his patient and consultants, are with the insurance carrier.

The Commission has the ultimate authority, but not the present capability to process all claims in detail at an administrative level.

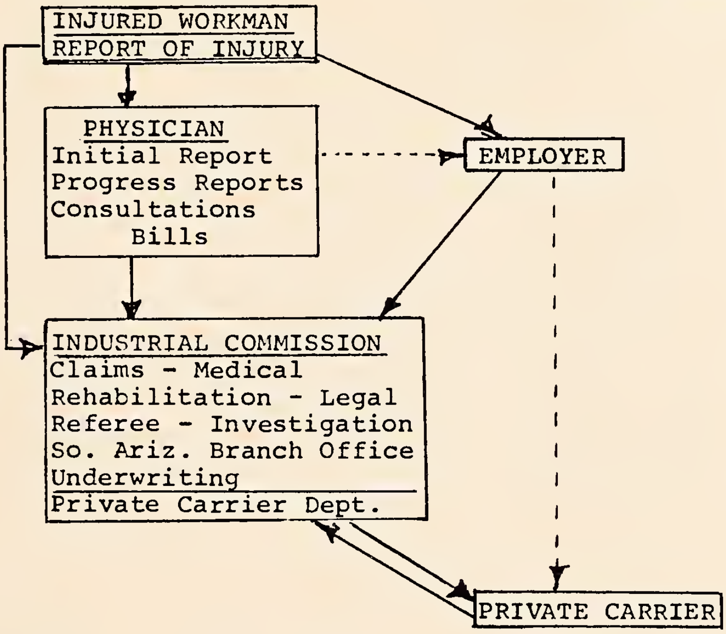
STATE COMPENSATION FUND

The State Compensation Fund formerly directed by The Industrial Commission, is now a separate public agency which is in effect an insurance company underwriting workmen's compensation insurance in competition with private insurance carriers and self-insured employers. It is directed by a three-member Board of Directors who are policyholders and who are appointed by the Governor, and who are not full time state employees. They employ a manager as chief executive. The income of the State Fund is derived entirely from premium income and from investment of reserves controlled by an Investment Committee composed of the Chairman of the Board of Directors of the State Fund, the Manager of the State Fund, and three members also appointed by the Governor. In all other respects it has the duties and responsibilities of other insurance carriers which are licensed and regulated by the Director of Insurance, another public officer.

On the basis of gross premium income, the State Compensation Fund is the largest single underwriter of workmen's compensation insurance in the state, and consequently may be somewhat more capable of providing a broader spectrum of services to insured employers and injured workmen. These include earlier identification of those claimants requiring comprehensive rehabilitation services which will be described in detail in later sections of this guide.

BEFORE JANUARY 1, 1969

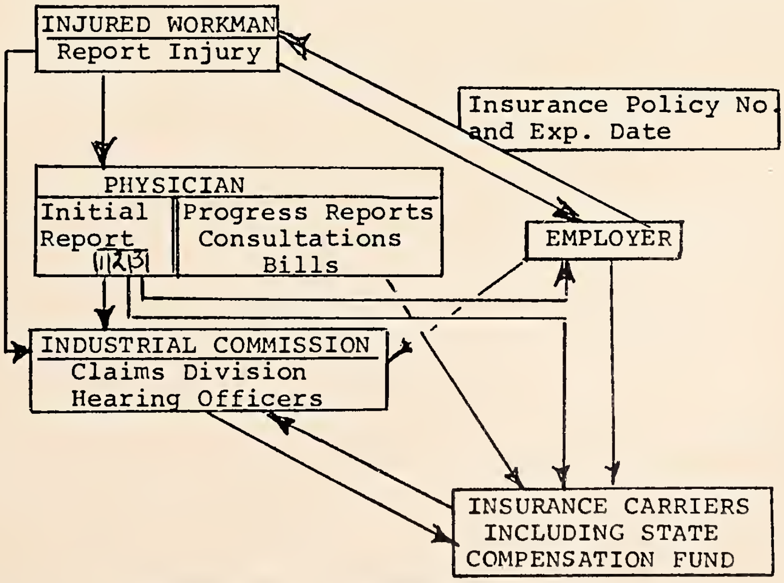
ICA:
1-Directed State
  Compensation Fund
2-Accepted or
  Denied Claims
3-Reopened Claims
4-Authorized
    Physical Therapy
    Injections
    Surgery
    Consultation
    Change of Physicians
    Claimants Leaving State
5-Adjudicated All Claims
6-Determined Loss of
  Earning Capacity
7-Made Scheduled
  Disability Awards
8-Paid Compensation
  and Medical Bills
  on SCF Cases



AFTER DECEMBER 31, 1968

ICA:
1-Adjudicates All Claims
2-Authorizes Claimant to
  Change Physicians or
  Leave the State
3-Determines Loss of
  Earning Capacity

INSURANCE CARRIERS:
1-Accept or Deny Claims
2-Pay Compensation and
  Medical Bills
3-Authorize Physical
  Therapy, Injections,
  Surgery, Consultations



Topics Of Current Medical Interest

STATE ADOPTS NEW REGULATIONS REGARDING IMPORTATION OF CHILDREN FOR ADOPTION

INTER-STATE PLACEMENT OF CHILDREN FOR ADOPTION

Reciprocal Agreements Between State Welfare Departments

Reciprocal agreements between State Departments of Public Welfare make it possible to place children in adoptive homes across state lines when a suitable home is not available for the child in his own state. Throughout the entire procedure, the child, the natural and the adoptive parents are given the same protection as in intra-state adoptive placements. Approval for the placement of a child for adoption in or out of the state is given by the Director of Child Welfare Services prior to the placement of the child. In out-of-state adoptions, the county department may obtain a certified birth certificate for the adoptive parents.

Local Placement of Out-of-State Children by Persons or Organizations

With certain exceptions, any effort to bring a child under age 18 into the state for adoption or other placement must be approved by the Director of Child Welfare. Exceptions include child's parents, stepparents, grandparents, brothers, sisters or first degree aunts and uncles. Their purposes for bringing the child into the state must be for placement of the child in their own homes.

Before approval will be given, the sponsoring person or organization must conform to all Department regulations and laws of the state.

The Department shall be responsible for the protection of children, approved to enter the state for placement, while they remain here and until they are adopted or reach the age of 18.

Approval for Licensed Child Welfare Agencies

Child Welfare agencies licensed by the Department to make foster home and adoption placements must submit an inter-state agreement to the Child Welfare Director for approval.

Approval for Unlicensed Organizations and Individuals

All unlicensed individuals or organizations must file a $1,000 bond with the Department before approval can be given. Conditions of the bond shall stipulate the child will not become a public charge or, in the opinion of the Child Welfare Director, become a menace to the community prior to adoption or becoming of legal age.

The proposed placement home must be eligible for approval by the Department according to its standards for foster homes.

Procedures

The Child Welfare Director shall be notified of intent to bring a child into the state on DPW-406, Application to Adopt – Provide Foster Care. Application can also be made by letter. It must specify the intention of the writer to bring a child into the state for placement. At the same time, it must include the name, age and personal description of the child, also the name and address of the placement home and other information specifically required by the placement.

If the placement home is approved by the Department, the applicant will be asked to file bond. Approval to bring the child itno the state will be acknowledged by the Child Welfare Director on form DPW-410, Foster Family Home License.

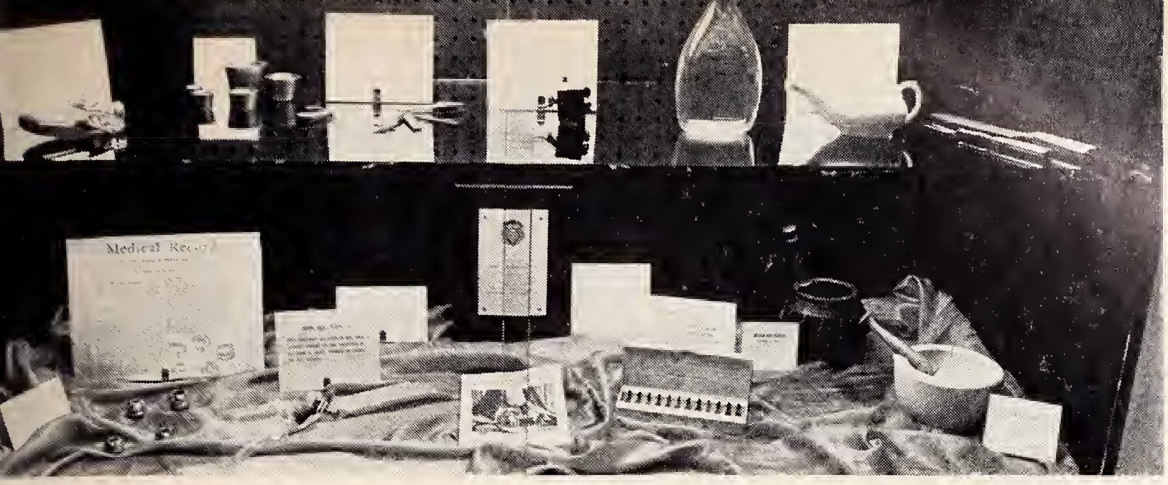
Letters to Editor

Dear Dr. Flynn:

I read the President's Page in the May 1969, issue of Arizona Medicine with pride. You have put into a few words what both medicine and nursing are striving to achieve, "working for the benefit of the patient." The comments about the educational programs were clear. Communication can do much to asist us toward our goals. I appreciate your message.

Thank you for featuring the University of Arizona College of Nursing in this issue.

Sincerely,
Sister Myrtle, R.N.
Director of Nursing
St. Joseph's Hospital
Tucson



MEDICAL HISTORY

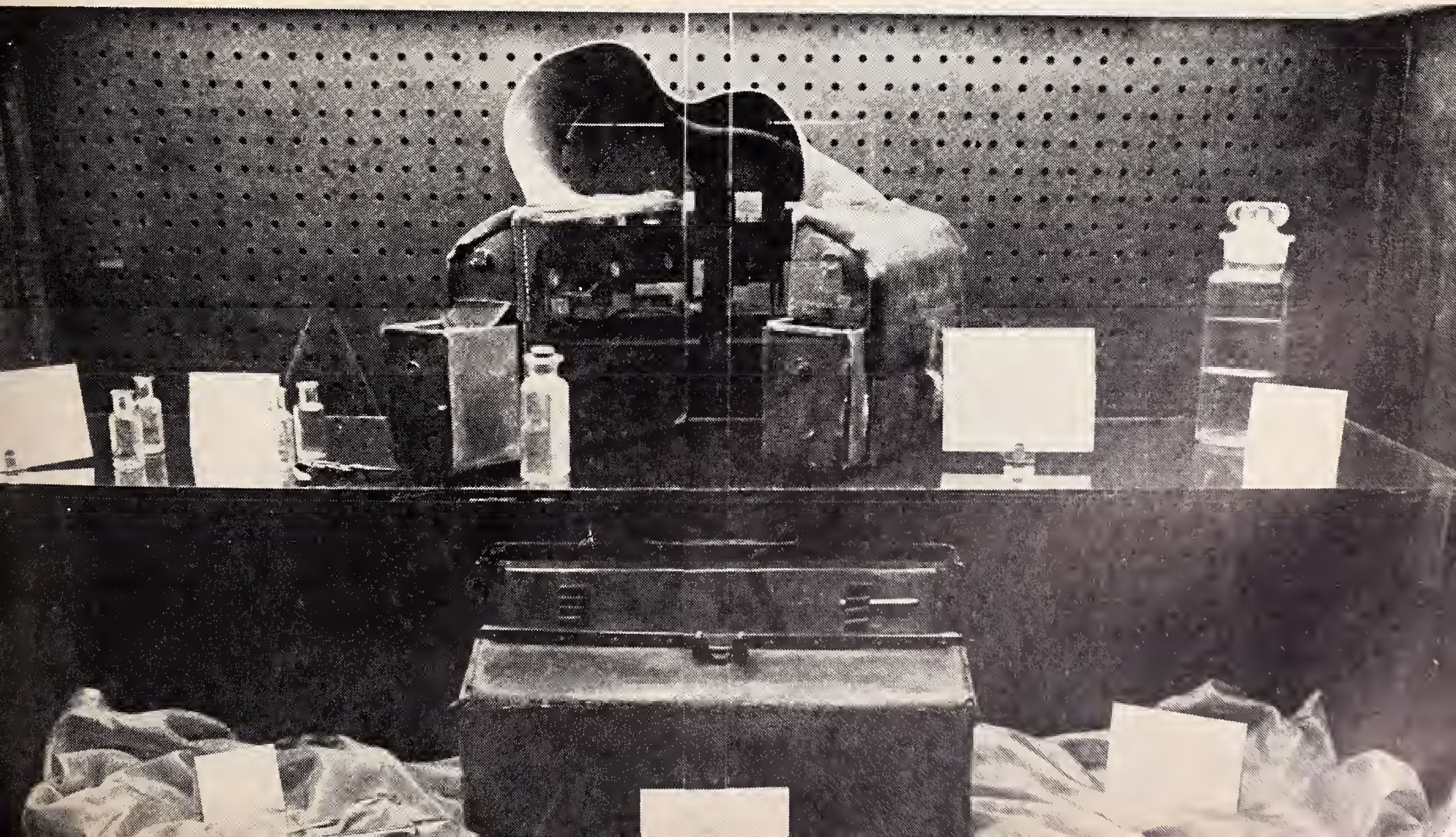
The paraphenalia of frontier medicine was the subject of an exhibit recently displayed in the Library of the College of Medicine at the University of Arizona. Drawn mainly from the collections of Mrs. Audrey Stevens, of Kearny, Arizona, the exhibit included such items as medical saddle bags dating from 1875 and associated with the Nogales area; surgical instruments from the turn of the century; and various types of "bleeders" from the 1700's and 1800's.

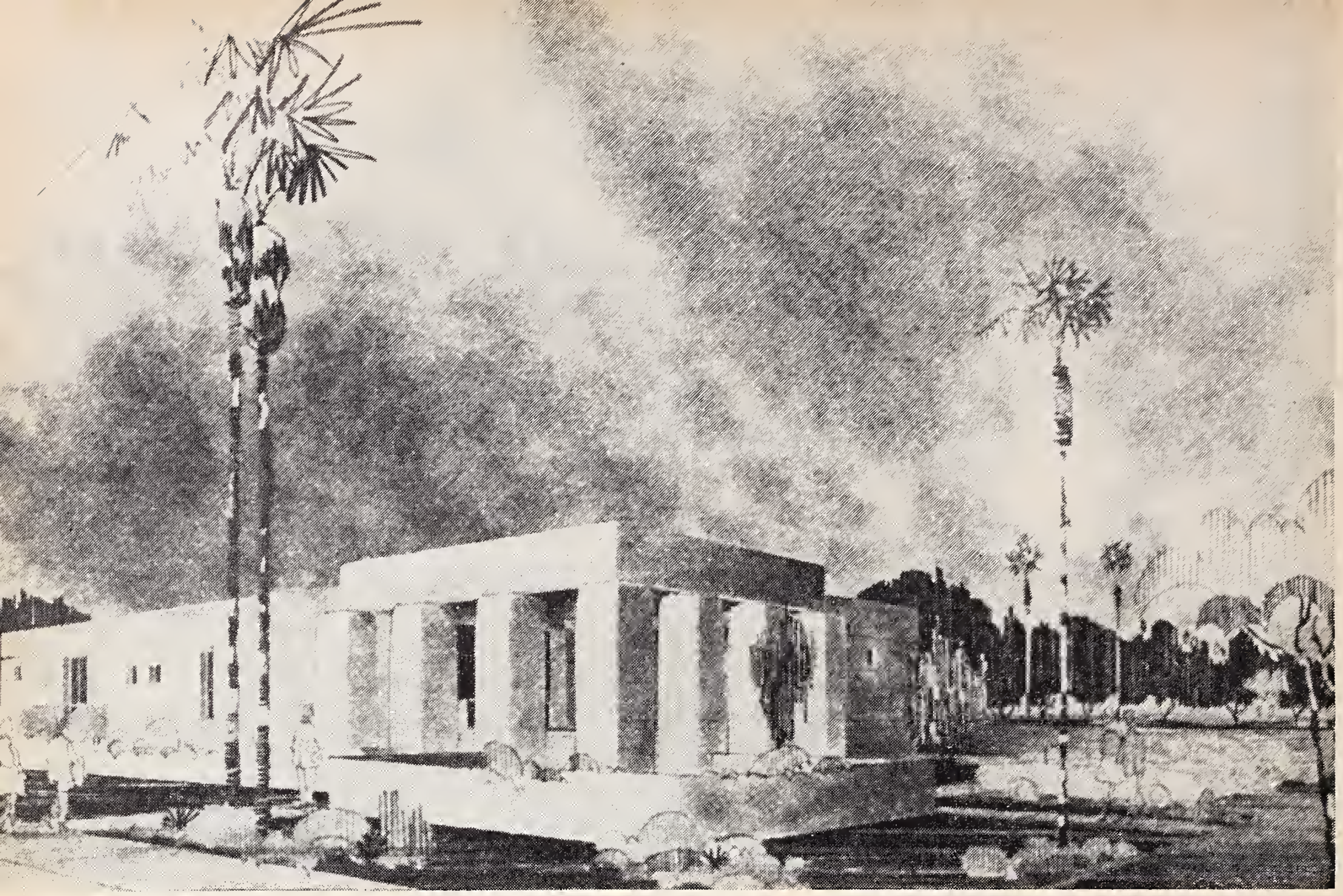
President George Washington was the most famous patient to be bled by an instrument similar to the bleeders that were on display. Physicians, 100 years later, were of the opinion that President Washington might have recovered from his case of pneumonia had he not been weakened from being bled so frequently. Please note: Bleeders were used on patients bfore the invention of anaesthesia.

A silver urine flask from 1815, donated to the Arizona Medical Association by Dr. Paul B. Jarrett, and now a part of the Medical Association's Historical Collection at the College of Medicine, was a part of the display. Men using flasks such as this urinal were suffering from prostate trouble. Dr. George Godfellow, of Tombstone and Tucson fame, was one of the first surgeons to perform a prostatectomy (1891). Dr. Goodfellow was often referred to as the "Father of Prostatectomy."

Other items of interest included feeding utensils from frontier days, an early 20th century set of drugs for the "cure" of narcotics addicts, and a set of "Murphy buttons" (an 1892 invention designated to replace suturing in some abdominal operations), these last two items having been formerly owned by the late Dr. James M. Walsh of Ray and Jerome, Arizona.

This is just the beginning of the Arizona Medical Association's Historical Collection. Should you be interested in contributing to this collection, please contact Dave Bishop, Librarian, College of Medicine, University of Arizona, Tucson 85721.





YOUR NEW HEADQUARTERS

After the 1968 House of Delegates meeting when the authorization was given to build a new headquarters building for ArMA, President Arthur V. Dudley, Jr. appointed a building committee to carry out the intent of the House. This committee was made up of Doctors Philip Dew, Arthur Dudley, Arnold Dysterheft, Richard Flynn, John Heileman, Fred Landeen, Arthur Nelson, Robert Price and Woodson Young. This committee has met frequently since that time and will report its decisions to the membership in this column.

We first retained the services of Mr. Frank Kelly, well-known real estate appraiser of Phoenix. Under his direction we considered many plots of ground in the "north central corridor" of Phoenix as the site of this new headquarters. This is an area between McDowell Road on the south, Bethany Home Road on the north, Seventh Avenue on the west, and Seventh Street on the east. We finally selected a plot on Bethany Home Road near Seventh Avenue, with a 200' frontage and 200' depth. This property was rezoned for our purposes and purchased at a price of $0.75 per square foot.

The committee next met with Dr. James Ellmore, Dean of the College of Architecture, Arizona State University, regarding architect selection. Acting upon his advice and after considering some twenty firms, we interviewed representatives of six major architectural offices regarding our proposed building. After these interviews we selected the firm of Bennie M. Gonzales Associates to prepare the plans.

At the time of this writing the plans have been completed, revised and finally approved by the Building Committee. Eight Phoenix contracting firms and two Tucson builders have been invited to bid on the job. Their study of our plans have been completed. The contract was awarded to Gilbert & Dolan Construction Company, Phoenix.

It is the intention of the committee to use this column to keep the membership informed of the progress of construction. Look for a further report next month.

Robert A. Price, M.D., Chairman
Ad Hoc Building Committee

BEFORE CONSTRUCTION STARTED

In Memoriam

Stanley W. Holton, M.D.
1897-1969

Dr. Stanley W. Holton died on March 25, 1969, at the age of 72. He had been in active practice for 35 years, retiring in 1958.

Dr. Holton came to Phoenix 27 years ago from Sedro Woolley, Washington. His career in Arizona included ward surgeon at the Veterans Hospital in Tucson, house surgeon at Memorial Hospital, plant physician at Reynolds Metals Co., from 1946 to 1954, industrial physician and surgeon at Bagdad Copper Co. from 1954 to 1958 when he retired and returned to Phoenix.

Born in Nevada, Mo., he was graduated from the University of Missouri in 1919 and Northwestern University Medical School in 1922. He interned at the Seattle City Hospital and spent a year at Northern Pacific Hospital at Tacoma, Washington. Later he served as ship's surgeon on the USS President Jefferson and returned from the Orient to a general practice at Sedro Woolley from 1924 to 1942.

He had been city health officer in Sedro Woolley and a member of the Skagit County Medical Society and served as its president and secretary. He also was a former president of the Rotary Club, a member of the Order of Eastern Star, a Masonic and Eagle lodge, all in Washington. Dr. Holton was a member of the Arizona and American Medical Associations and the Maricopa County Medical Society.

Survivors include his wife, Helen; a son, Stanley Jr. of Phoenix; his mother, Mrs. Gertrude B. Holton of Irving, Texas; a brother out of state; and one grandchild.

Maxwell R. Palmer, M.D.
1909-1969

Maxwell R. Palmer, M.D., Tucson, died on April 28, 1969, at the age of 59.

Dr. Palmer, a native of Joliet, Illinois, received his B.S. and M.D. degrees from Louisiana State University in New Orleans. His internship was completed at the U.S. Marine Hospital in San Francisco, and he was a resident physician at Stephens College in Columbia, Mo.

Dr. Palmer received postgraduate education in anesthesia at the University of Iowa. In 1939 he became student health physician at the University of Arizona, and two years later entered private practice.

From 1942 to 1946, Dr. Palmer served with the Army Air Corps as a flight surgeon, and was discharged with the rank of major. Since 1946 he practiced in Tucson.

He was a diplomate of the American Board of Anesthesiology, a member of the Pima County Medical Society, the Arizona Medical Association, the Arizona State Society of Anesthesiologists, and the American Medical Association. He also was first vice president of the American Society of Anesthesiologists.

Dr. Palmer is survived by his widow, Zeta, of Tucson; two sons, David K. and Maxwell R.; his mother, Mrs. Emaline Stutz Palmer; a brother, John D.; two sisters, Mrs. Roy Malmstead and Mrs. Marjorie Awe; and two grandchildren.

Medical History

TEST YOUR MEDICAL HISTORY I.Q.

(Turn to page 598 for answers)

	TRUE	FALSE
1. Paleopathology includes the study of abnormalities found in the remains of animals and man (fossils).	☐	☐
2. The paleolithic period ended in about 8,000 B.C.	☐	☐
3. Medicine of primitive cultures was instinctive, empirical, magical and priestly.	☐	☐
4. Trephination of the skull is probably the earliest operation of which we have tangible evidence.	☐	☐
5. Liver livination began in Arabia.	☐	☐
6. Hammurabi, the sixth king of Babylon, established the concept of the responsibility of the physician to society.	☐	☐
7. Imhotep was the outstanding Assyro-Babylonian medical personage.	☐	☐
8. The Edwin Smith Papyrus is the most important treatise on surgery of early antiquity.	☐	☐
9. The Egyptians had no materia medica.	☐	☐
10. Preventive medicine and social medicine were unknown to the Egyptians.	☐	☐
11. Acupuncture is of Chinese origin dating back to 2,700 B.C.	☐	☐
12. Monotheism and social hygiene are lasting early Hebrew contributions.	☐	☐
13. Susruta described rhinoplasty (nose repair) as early as the third century B.C.	☐	☐
14. The mortality rate in 140 wounds described in Homeric poems was ten percent.	☐	☐
15. Aesculapius was the legendary son of Apollo, inventor of the healing art.	☐	☐
16. Temples of Aesculapius became medical centers prior to Hippocrates.	☐	☐
17. The Golden Age of Greek Medicine occurred in the year 1,000 B.C.	☐	☐
18. Hippocrates taught that diseases are due to supernatural causes.	☐	☐
19. Hippocrates and his pupils wrote extensively.	☐	☐
20. Hippocrates had nothing to do with the School of Cos.	☐	☐
21. The Oath of Hippocrates taught human compassion and ethical standards.	☐	☐
22. Hippocrates has been termed the "Father of Medicine."	☐	☐
23. Gold dentures were made by the Etruscans.	☐	☐
24. Julius Caesar made physicians citizens, not slaves.	☐	☐
25. Galen was the outstanding physician of the Roman period.	☐	☐
26. Byzantium, Constantinople and Istanbul are names for the same place.	☐	☐
27. The Benedictine Rule was spread from Montecassino.	☐	☐
28. Avicenna was a genius of the Arabic culture.	☐	☐
29. Albucasis' book On Surgery condemned cautery in surgery.	☐	☐
30. The School of Salerno was mentioned as early as 848.	☐	☐
31. The School of Salerno maintained a close relationship with the Benedictine Abbey at Montecassino.	☐	☐
32. Universities began in the Middle Ages.	☐	☐
33. Theodoric of Bologna advised closure of wounds to reduce infection.	☐	☐
34. Guy deChauliac of Montpellier described the plague.	☐	☐
35. Italy was the center of culture and learning during the medieval period.	☐	☐
36. Astrology was scorned during the Middle Ages.	☐	☐
37. Gunshot wounds and their treatment began in the thirteenth century.	☐	☐

	TRUE	FALSE
38. Syphilis was named in 1530 by Galen.	☐	☐
39. The first scientific statement of the true nature of contagion was made by Fracastoro in 1546.	☐	☐
40. Paracelsus broke with the humoral theory of disease of Galen.	☐	☐
41. Artists were not involved in the early development of anatomy.	☐	☐
42. Andreas Vesalius was not the dominant figure in the field of anatomy in the Renaissance.	☐	☐
43. Ambroise Paré was the outstanding Renaissance surgeon.	☐	☐
44. Paré did not condemn the use of cautery or hot oil in surgery.	☐	☐
45. The period of the Renaissance marked the return of primitive medicine.	☐	☐
46. René Déescartes invented, in a way, reflex action.	☐	☐
47. Déscartes conceived the pineal gland to be the seat of the soul.	☐	☐
48. Francis Bacon developed inductive reasoning.	☐	☐
49. Anton van Leewenhoek described a large number of bacteria and protozoa.	☐	☐
50. William Harvey spurred physiology by discovering venous valves.	☐	☐
51. De Motu Cordis was written by Osler.	☐	☐
52. Harvey's work on the circulation of blood was classic.	☐	☐
53. The Age of Enlightenment is a term which has been applied to the eighteenth century.	☐	☐
54. France was the cultural leader during the eighteenth century.	☐	☐
55. The University of Leyden developed an outstanding medical center during the eighteenth century.	☐	☐
56. Hermann Boerhaave was the leading surgeon of his century.	☐	☐
57. The Old Vienna School of Medicine was established by Gerhard van Swieten of Leyden.	☐	☐
58. Giovanni Morgagni has been termed "The Father of Obstetrics."	☐	☐
59. Morgagni introduced an anatomical concept to pathology and medicine.	☐	☐
60. Scurvy was no problem after Lind first discussed its treatment.	☐	☐
61. Physiological surgery was introduced by John Hunter.	☐	☐
62. Vaccination was immediately accepted and popular.	☐	☐
63. Edward Jenner's work on smallpox, published in 1798, was met with controversy.	☐	☐
64. The classic experiment to record blood pressure was done in 1711 by Reverend Stephen Hales.	☐	☐
65. Antoine Lavoisier may be credited with naming, developing and understanding oxygen.	☐	☐
66. The stethoscope was developed by Francois Magendie in 1816.	☐	☐
67. Napoleon's famous surgeon, Larrey, invented "flying ambulances" – a principle in the care of battle injuries.	☐	☐
68. American medicine originated with the British colonists.	☐	☐
69. Herbs were the basis of materia medica for American Indians.	☐	☐
70. The Spanish were the first to organize medical schools and hospitals in America.	☐	☐
71. Early colonists in America were dependent upon governors, ministers and minor physicians for medical services.	☐	☐
72. Benjamin Franklin would not support the Pennsylvania Hospital which was established in 1851.	☐	☐
73. The first medical school in the colonies was established in Philadelphia in 1765.	☐	☐
74. Ninety percent of the deaths which occurred during the Revolutionary War were the result of disease; ten percent from battle casualties.	☐	☐
75. Contagiousness of Puerperal Fever, a medical classic in Obstetrics, was written by Oliver Wendell Holmes, Sr. in 1843.	☐	☐

	TRUE	FALSE
76. Ether anesthesia was introduced by Ambroise Paré in Paris.	☐	☐
77. The first ovarian cysts were successfully removed by Euphraim McDowell in Danville, Kentucky, beginning in 1809.	☐	☐
78. Claude Bernard was a famous French surgeon.	☐	☐
79. Cellularpathologie, published by Virchow in 1858, challenged the two thousand-year-old humoral theory of disease.	☐	☐
80. Wilhelm C. Roentgen discovered x-rays in Russia in 1810.	☐	☐
81. The use of carbolic acid spray to sterilize the operative field was introduced in 1865 by Joseph Lister.	☐	☐
82. Pasteurization was introduced in 1864 in connection with destroying parasitic growths by heating wine to 50-60°C by Pasteur.	☐	☐
83. Sickness killed more than four times the men who died as the result of battle injuries during the Civil War.	☐	☐
84. William Henry Welch, the first full-time pathologist in the U. S., perfected grape juice.	☐	☐
85. Osler's Principles and Practice of Medicine, published in 1892, was not only a classic, but influenced Rockefeller philanthropy.	☐	☐
86. Alfred Nobel's will of 1895 created prizes "to those who during the preceding year shall have conferred the greatest benefit on mankind."	☐	☐
87. Yellow Fever, its cause and cure, was elucidated by Benjamin Rush.	☐	☐
88. Construction of the Panama Canal was not feasible until Yellow Fever could be controlled.	☐	☐
89. Spain has generously supported her scientists.	☐	☐
90. Ramon y Cajal received the Nobel Prize in 1906 for his pioneer work in the study of the fine anatomy of the nervous system.	☐	☐
91. Rickettsial diseases are transmitted by lice and ticks.	☐	☐
92. Vitamins are amines.	☐	☐
93. Sigmund Freud was the founder of modern neurological surgery.	☐	☐
94. Harvey Cushing, a neurosurgeon, did much to develop endocrinology.	☐	☐
95. World War I was the first war of magnitude in history in which the mortality from battle casualties exceeded that of communicable diseases.	☐	☐
96. "Shell-shock" of World War I and "Combat-fatigue" of World War II, are essentially the same entities.	☐	☐
97. Insulin was discovered in 1922 by Banting and Best.	☐	☐
98. Sulfa drugs, electroencephalography and electron microscopy originated in Russia prior to World War II.	☐	☐
99. Citizens of the United States spend approximately the same for recreation, exclusive of beverages and tobacco, as they do for medical care and death expenses.	☐	☐
100. The challenges and opportunities in medicine are continuing at an ever increasing pace.	☐	☐

SEE PAGE 598 FOR CORRECT ANSWERS AND HOW TO SCORE

FOURTH SUMMER SEMINAR
COCONINO COUNTY MEDICAL SOCIETY and the UNIVERSITY OF ARIZONA COLLEGE OF MEDICINE

August 9-10, 1969
Coconino County Health Department Auditorium
Fort Valley Road, Flagstaff

Saturday, August 9

8:00	Registration
9:00	Introduction: Coconino County Medical Society
9:20	The Management of Burns — Dr. Peacock
9:40	Non-neoplastic and Precancerous Lesions of the Vulva — Dr. Davis
10:00	The Diagnosis and Management of Secondary Amenorrhea — Dr. Christian
10:20	Coffee Break
10:40	Evaluation and Medical Diagnosis in Peripheral Nerve Disease — Dr. Buchsbaum
11:00	The Use of Digitalis in Acute Myocardial Infarction — Dr. Marcus
11:20	Digitalis Therapy in the Elderly — Dr. Ewy
11:40	Diagnosis of Heart Disease by Altering Murmurs with Drugs and Postural Changes — Dr. O'Rourke
12:00	Luncheon Address: Arizona's New Medical School: A Progress Report — Dr. DuVal

Sunday, August 10

9:00	The "Diagnosis" of Anemia — Dr. Thorup
9:20	Drug-Induced Immune Hemolytic Anemia — Dr. Boyer
9:40	Lactose Intolerance and Intestinal Lactase Deficiency — Dr. Krone
10:00	Granulocyte Function: Normal and Abnormal — Dr. Fulginiti
10:20	Clinical Evaluation of Antibiotic Sensitivity Studies — Dr. Rifkind
10:40	Coffee Break
11:00	The Treatment of Acute Respiratory Failure — Dr. Kettel
11:20	Family Practice and Community Medicine — Dr. Abrams
11:40	A Progress Report on the Arizona Regional Medical Program — Dr. Melick
12:00	Adjournment

Guest Faculty:

Earle J. Peacock, M.D.
Professor and Head
Department of Surgery

John R. Davis, M.D.
Associate Professor
Department of Pathology

C. Donald Christian, M.D.
Associate Professor
Department of Obstetrics and Gynecology

Harvey Wm. Buchsbaum, M.D.
Assistant Professor
Department of Internal Medicine

Frank I. Marcus, M.D.
Professor of Medicine
Chief, Cardiology Section
Department of Internal Medicine

Gordon A. Ewy, M.D.
Assistant Professor
Department of Internal Medicine

Robert A. O'Rourke, M.D.
Assistant Professor
Department of Internal Medicine

Merlin K. DuVal, M.D.
Dean
College of Medicine

Oscar A. Thorup, M.D.
Professor and Head
Department of Internal Medicine

John T. Boyer, M.D.
Associate Professor
Chief, Immunology Section
Department of Internal Medicine

Charles L. Krone, M.D.
Assistant Professor
Chief, Gastroenterology Section
Department of Internal Medicine

Vincent A. Fulginiti, M.D.
Professor and Head
Department of Pediatrics

David Rifkind, Ph.D., M.D.
Professor and Head
Department of Microbiology
Professor of Medicine
Chief, Infectious Diseases Section
Department of Internal Medicine

Louis J. Kettel, M.D.
Associate Professor
Department of Internal Medicine

Herbert Abrams, M.D.
Professor and Head
Department of Community Medicine

Dermont W. Melick, M.D.
Coordinator
Arizona Regional Medical Program
Professor
Department of Surgery

AAGP CATEGORY I APPROVAL GRANTED.

For further information regarding program and motel reservations contact: Robert E. Westfall, M.D., Secretary, Coconino County Medical Society, 1355 North Beaver, Flagstaff, Arizona 86001

6TH NATIONAL CANCER CONFERENCE – NOTES

September 1968, Denver

Preventative measures against metastasis and local recurrence in cancer surgery.

In the experimental animal trauma associated with the administration of an anesthetic will result in the development of two times as many tumors with the injection of cancer cells into the host as would have occurred had the cells been injected without the administration of an anesthetic or the precipitation of trauma.

In colon surgery, 1 — Ligation of the bowel; 2 — Ligation of the vascular pedicle prior to mobilization; 3 — Use iodized suture material. This technique in Class C lesions will result in almost twice as many survivals, that is a step-up from 28 to 58%.

In cancer of the breast, the local recurrence rate is not effected by wound irrigation. He does advocate simultaneous chemotherapy with nitrogen mustard showing probably 11% improvement rate in 7 to 12 years survival curves in two groups of patients, that is the premenopausal female with negative nodes and the post-menopausal female with positive nodes.

Gerald O. McDonald, M.D.
Professor of Surgery, University of
Illinois College of Medicine

Answers to Medical History I.Q. Test on Pages 594-596

Subtract errors from 100 to obtain your score. How do you rate, compared to:
ASU History of Medicine Final Examination (35 students) Scores 64-95..Av. 82.8
Junior, Camelback High School Science Major ....Av. 82
Medical History Club of Phx. (8 M.D.'s with 1 abstaining) Scores 48-90..Av. 79.3

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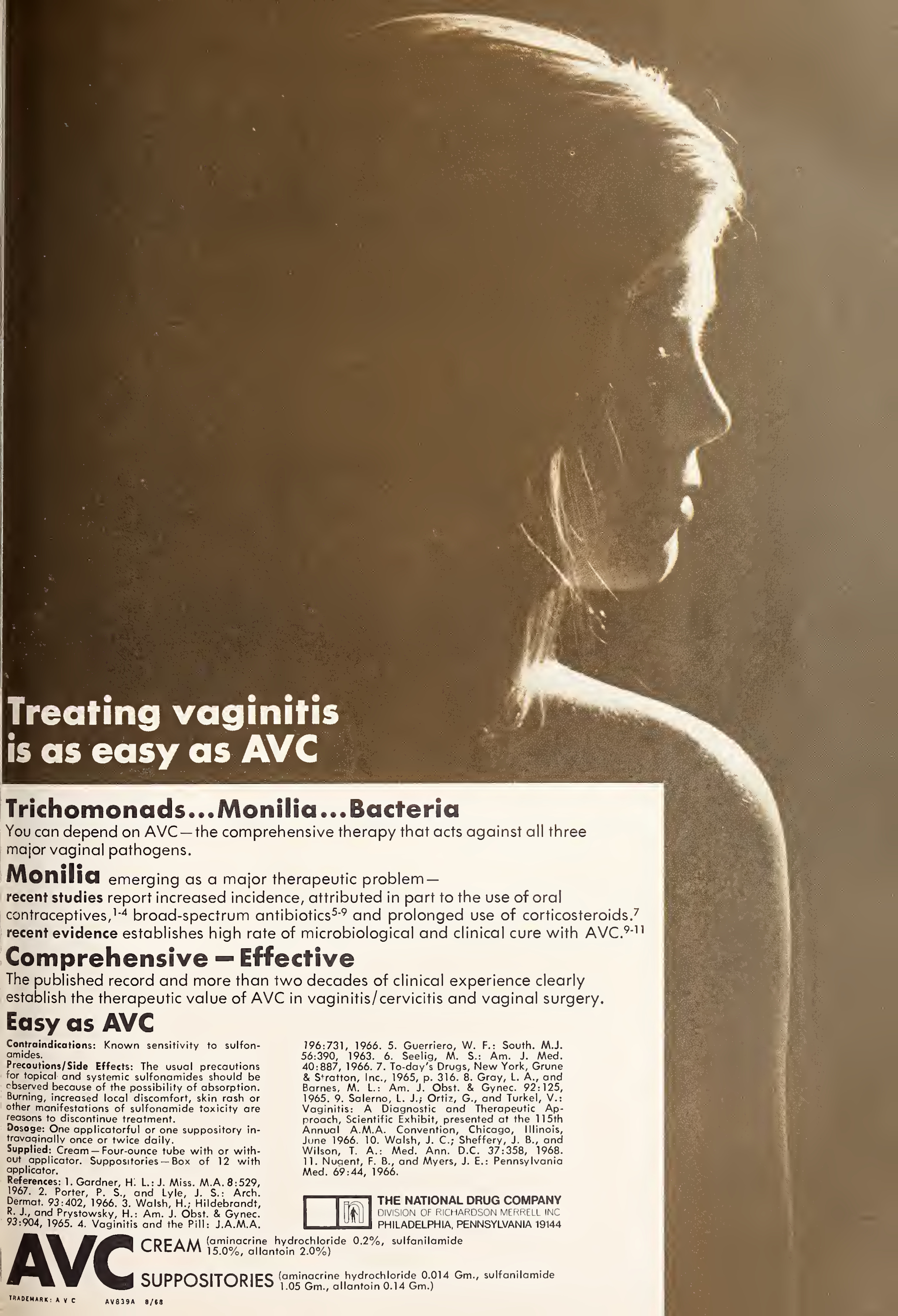

Treating vaginitis is as easy as AVC

Trichomonads...Monilia...Bacteria

You can depend on AVC—the comprehensive therapy that acts against all three major vaginal pathogens.

Monilia emerging as a major therapeutic problem—

recent studies report increased incidence, attributed in part to the use of oral contraceptives,[1-4] broad-spectrum antibiotics[5-9] and prolonged use of corticosteroids.[7]

recent evidence establishes high rate of microbiological and clinical cure with AVC.[9-11]

Comprehensive—Effective

The published record and more than two decades of clinical experience clearly establish the therapeutic value of AVC in vaginitis/cervicitis and vaginal surgery.

Easy as AVC

Contraindications: Known sensitivity to sulfonamides.

Precautions/Side Effects: The usual precautions for topical and systemic sulfonamides should be observed because of the possibility of absorption. Burning, increased local discomfort, skin rash or other manifestations of sulfonamide toxicity are reasons to discontinue treatment.

Dosage: One applicatorful or one suppository intravaginally once or twice daily.

Supplied: Cream—Four-ounce tube with or without applicator. Suppositories—Box of 12 with applicator.

References: 1. Gardner, H. L.: J. Miss. M.A. 8:529, 1967. 2. Porter, P. S., and Lyle, J. S.: Arch. Dermat. 93:402, 1966. 3. Walsh, H.; Hildebrandt, R. J., and Prystowsky, H.: Am. J. Obst. & Gynec. 93:904, 1965. 4. Vaginitis and the Pill: J.A.M.A. 196:731, 1966. 5. Guerriero, W. F.: South. M.J. 56:390, 1963. 6. Seelig, M. S.: Am. J. Med. 40:887, 1966. 7. To-day's Drugs, New York, Grune & Stratton, Inc., 1965, p. 316. 8. Gray, L. A., and Barnes, M. L.: Am. J. Obst. & Gynec. 92:125, 1965. 9. Salerno, L. J.; Ortiz, G., and Turkel, V.: Vaginitis: A Diagnostic and Therapeutic Approach, Scientific Exhibit, presented at the 115th Annual A.M.A. Convention, Chicago, Illinois, June 1966. 10. Walsh, J. C.; Sheffery, J. B., and Wilson, T. A.: Med. Ann. D.C. 37:358, 1968. 11. Nugent, F. B., and Myers, J. E.: Pennsylvania Med. 69:44, 1966.

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TRADEMARK: A V C   AV839A 8/68

in trauma

new Orenzyme® Bitabs

One tablet q.i.d.

Trypsin: 100,000 N.F. Units, Chymotrypsin: 8,000 N.F. Units.; equivalent in tryptic activity to 40 mg. of N.F. trypsin

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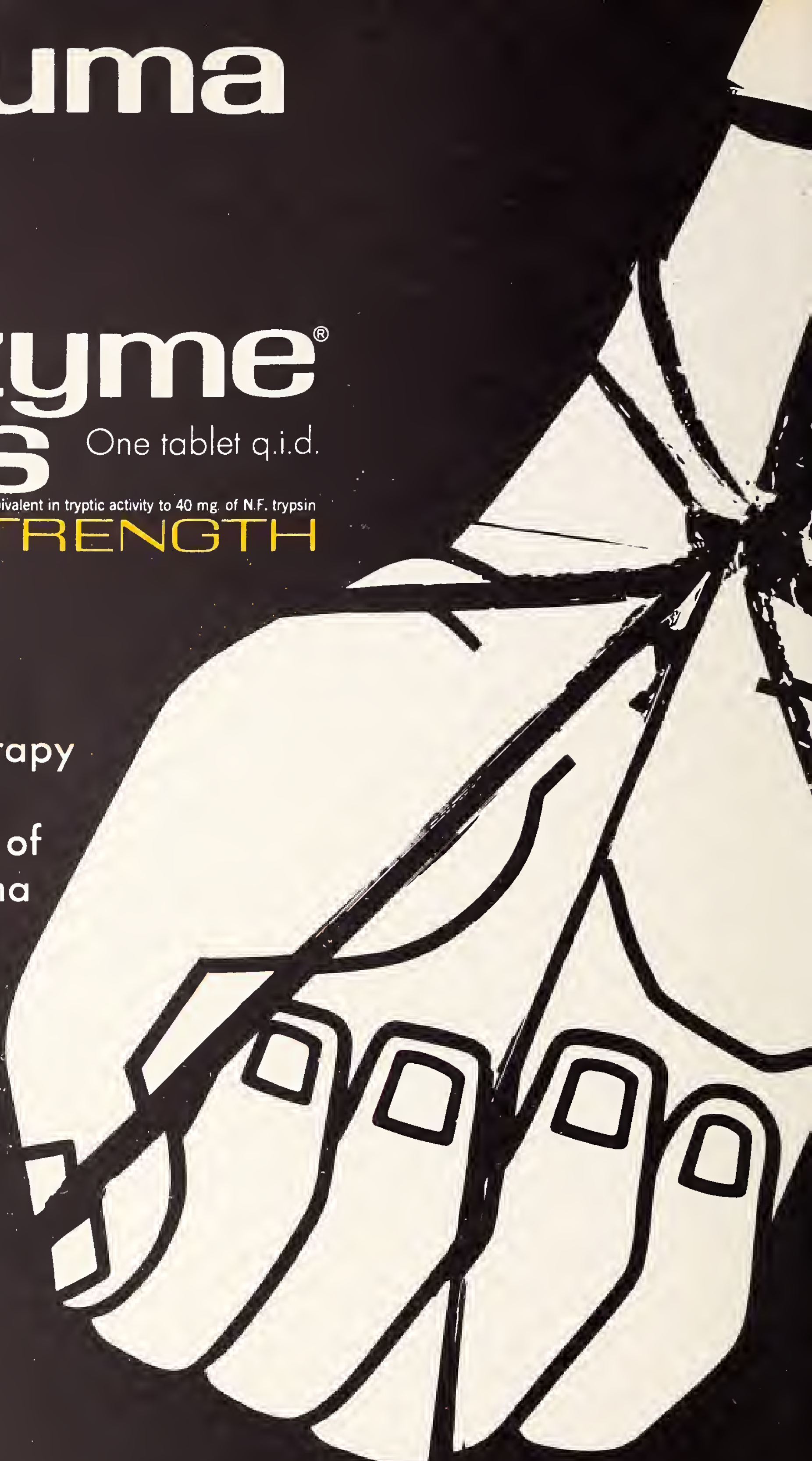

Proteolytic enzyme therapy specifically indicated for the rapid resolution of inflammation and edema as adjunctive therapy in accidental and surgical trauma.

1 tablet q.i.d. provides recommended therapeutic dose at lower cost.

Description: ORENZYME BITABS offers the therapeutic effects of trypsin in an oral form as adjunctive therapy for the rapid resolution of inflammation and edema. ORENZYME BITABS is convenient to use, promotes patient cooperation and is ideally suited for maintenance therapy following parenteral trypsin.

Indications: When used as adjunctive therapy for the rapid resolution of inflammation and edema, good results have been obtained in:

☐ Accidental Trauma
☐ Postoperative Tissue Reactions.

Other conventional measures of treatment should be used as indicated. In infection, appropriate anti-infective therapy should be given.

Contraindications: ORENZYME BITABS should not be given to patients with a known sensitivity to trypsin or chymotrypsin.

Precautions: It should be used with caution in patients with abnormality of the blood clotting mechanism such as hemophilia, or with severe hepatic or renal disease. Safe use in pregnancy has not been established.

Adverse Reactions: Adverse reactions with ORENZYME have been reported infrequently. Reports include allergic manifestations (rash, urticaria, itching), gastrointestinal upset and increased speed of dissolution of animal-origin surgical sutures. There have been isolated reports of anaphylactic shock, albuminuria and hematuria. Increased tendency to bleed has also been reported but, in controlled studies, it has been seen with equal incidence in placebo-treated groups. (See Precautions.) It is recommended that if side effects occur medication be discontinued.

Dosage: One tablet q.i.d.

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TRADEMARK: BITABS U.S. PATENT NO. 3,004,893 4/69 0-821A

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(SODIUM BUTABARBITAL)

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After 30 years of clinical use . . . still a first choice among many physicians for dependability, safety and economy in mild to moderate anxiety.

Contraindications: Porphyria or sensitivity to barbiturates.

Precautions: Exercise caution in moderate to severe hepatic disease. Elderly or debilitated patients may react with marked excitement or depression.

Adverse Reactions: Drowsiness at daytime sedative dose levels, skin rashes, "hangover" and systemic disturbances are seldom seen.

Warning: May be habit forming.

Usual Adult Dosage: As a daytime sedative, 15 mg. (¼ gr.) to 30 mg. (½ gr.) t.i.d. or q.i.d.

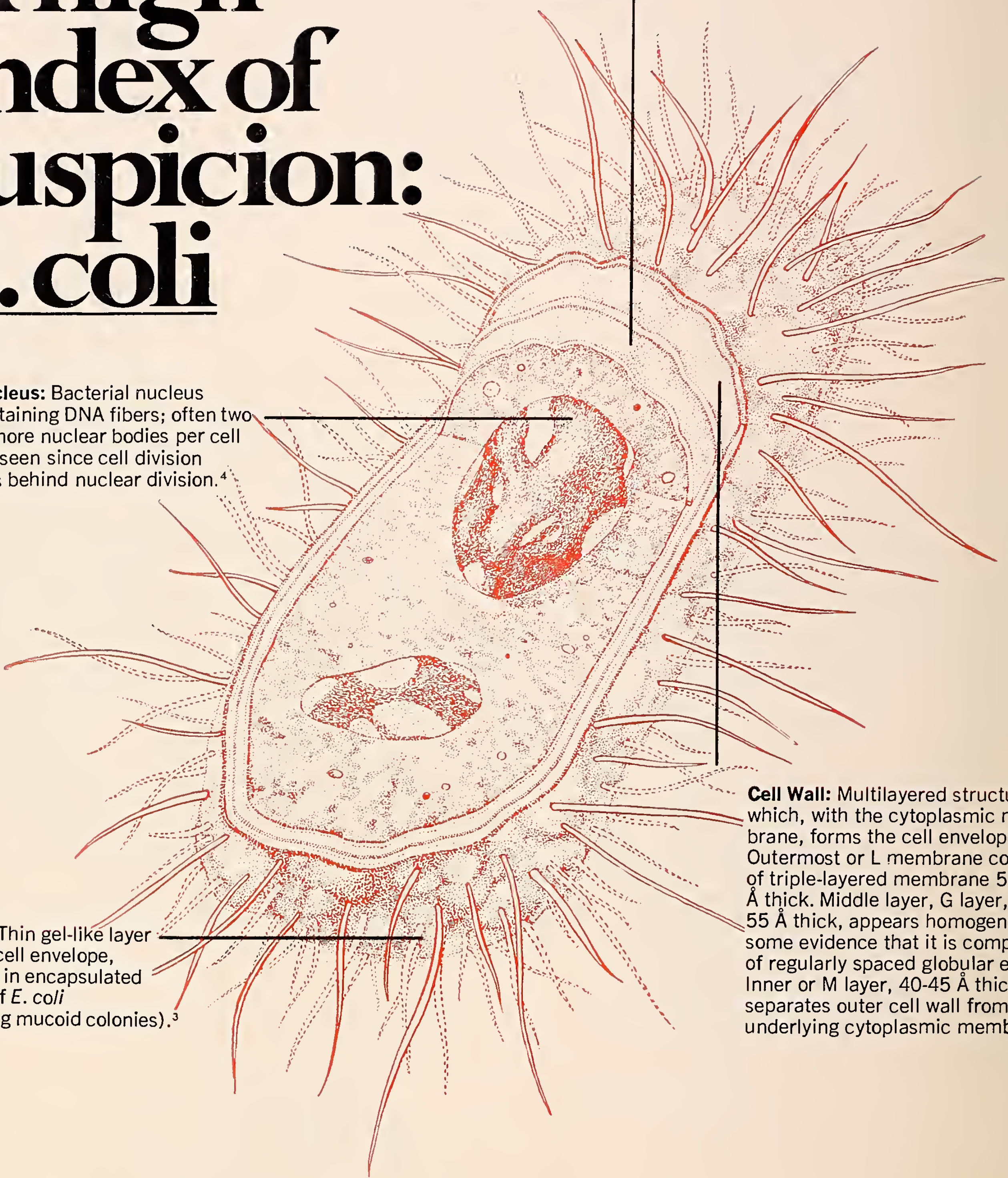
Available for daytime sedation: Tablets, 15 mg. (¼ gr.), 30 mg. (½ gr.); Elixir, 30 mg. per 5 cc. (alcohol 7%).

BUTICAPS® [Capsules Butisol Sodium (sodium butabarbital)] 15 mg. (¼ gr.), 30 mg. (½ gr.).

McNEIL

McNeil Laboratories, Inc., Fort Washington, Pa.

A high index of suspicion: E. coli



Cytoplasmic Membrane: Triple-layered membrane, 50-55 Å thick.[3]

Nucleus: Bacterial nucleus containing DNA fibers; often two or more nuclear bodies per cell are seen since cell division lags behind nuclear division.[4]

Cell Wall: Multilayered structure which, with the cytoplasmic membrane, forms the cell envelope. Outermost or L membrane consists of triple-layered membrane 50-55 Å thick. Middle layer, G layer, 50-55 Å thick, appears homogenous bu some evidence that it is composed of regularly spaced globular elemen Inner or M layer, 40-45 Å thick, separates outer cell wall from underlying cytoplasmic membrane.[3]

Capsule: Thin gel-like layer covering cell envelope, occurring in encapsulated variants of *E. coli* (producing mucoid colonies).[3]

Artist's rendition of E. coli. *As with most strains of* E. coli, *these have flagella and are m*

How high is the "index of suspicion" for *E. coli* in urinary tract infections?

Recently it has been estimated that about 86 per cent of positive cultures in first attacks of urinary tract infection are *E. coli*.[1] It has been similarly noted that "The coliform group, especially *E. coli*, accounts for approximately 90 per cent of initial infections...."[2]

Consider wide-spectrum Gantanol® (sulfamethoxazole) for its high "index of confidence" —its proven effectiveness against *E. coli* and other sensitive gram-negative and gram-positive pathogens. Therapeutic levels of Gantanol in blood and urine are achieved within 2 hours after a 2-Gm starting dose, with ready diffusion into interstitial fluids. Responsive infections generally clear within 5 to 7 days, with relief of symptoms usually seen within 24 to 48 hours.

Gantanol (sulfamethoxazole) also earns its high "index of confidence" because Gantanol therapy is relatively free from complications, including the problem of bacterial resistance or superinfection.

Convenient, economical dosage schedule: *b.i.d.*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute and chronic urinary tract, respiratory and soft tissue infections due to susceptible microorganisms; prophylactically following diagnostic instrumental procedures on genitourinary tract.

Contraindicated in sulfonamide-sensitive patients, pregnant females at term, premature infants, or newborn infants during first 3 months of life.

Warnings: Use only after critical appraisal in patients with liver or renal damage, urinary obstruction or blood dyscrasias. Deaths reported from hypersensitivity reactions, Stevens-Johnson syndrome, agranulocytosis, aplastic anemia and other blood dyscrasias. In closely intermittent or prolonged therapy, blood counts and liver and kidney function tests should be performed. Clinical data insufficient on prolonged or recurrent therapy in chronic renal diseases of children under 6 years.

Precautions: Occasional failures may occur due to resistant microorganisms. Not effective in virus and rickettsial infections. Sulfonamides not recommended for therapy of acute infections caused by group A beta-hemolytic streptococci. At present, penicillin is drug of choice in acute group A beta-hemolytic streptococcal infections; although Gantanol has produced favorable bacteriologic conversion rates in this infection, data insufficient on long-term follow-up studies as to its effect on sequelae of rheumatic fever or acute glomerulonephritis. If other treatment cannot be used and Gantanol is employed in such infections, *important that therapy be continued in usual recommended dosage for at least 10 days.* Observe usual sulfonamide therapy precautions, including adequate fluid intake. Use with caution if history of allergies and/or asthma. Follow closely patients with renal impairment since this may cause excessive drug accumulation. Need for indicated local measures or surgery not obviated in localized infections.

Adverse Reactions: Depending upon the severity of the reaction, may withdraw drug in event of headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, Stevens-Johnson syndrome, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

Dosage: *Adults*—2 Gm (4 tabs or teasp.) initially, then 1 Gm b.i.d. or t.i.d. depending upon severity of infection. *Children*—0.5 Gm (1 tab or teasp.) / 20 lbs initially, followed by 0.25 Gm / 20 lbs b.i.d.

How Supplied: *Tablets*, 0.5 Gm, bottles of 50. *Suspension*, 10%, 0.5 Gm / teasp, bottles of 16 oz.

References: 1. Vernier, R. L., in Patient Care Feature: *Patient Care, 1*:20 (Feb.) 1967. **2.** Beeson, P. B.: "The Infectious Diseases," in Beeson, P. B., and McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Philadelphia, W. B. Saunders Company, 1967, p. 230. **3.** De Petris, S.: *J. Ultrastruct. Res., 12*:247, 1965. **4.** Davis, B.D., *et al.*: *Microbiology*, New York, Hoeber Medical Division, Harper & Row, Publishers, 1967, pp. 39-41.

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Tetracycline HCl—Antihistamine—Analgesic Compound

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In tetracycline-sensitive bacterial infection complicating respiratory allergy, ACHROCIDIN brings the treatment together in a single prescription—prompt relief of headache and congestion together with effective control of the organisms frequently responsible for complications leading to prolonged disability in the susceptible patient.

For children and elderly patients you may prefer caffeine-free ACHROCIDIN Syrup. Each 5 cc contains: ACHROMYCIN (Tetracycline) equivalent to Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Salicylamide 150 mg.; Ascorbic Acid (C) 25 mg.; Pyrilamine Maleate 15 mg.

Contraindications: Hypersensitivity to any component.

Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.

Precautions: Drowsiness, anorexia, slight gastric distress can occur. In excessive drowsiness, consider longer dosage intervals. Persons on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity* reactions—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

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It is an anticholinergic drug without narcotic properties. Side effects are usually mild.

LAKESIDE

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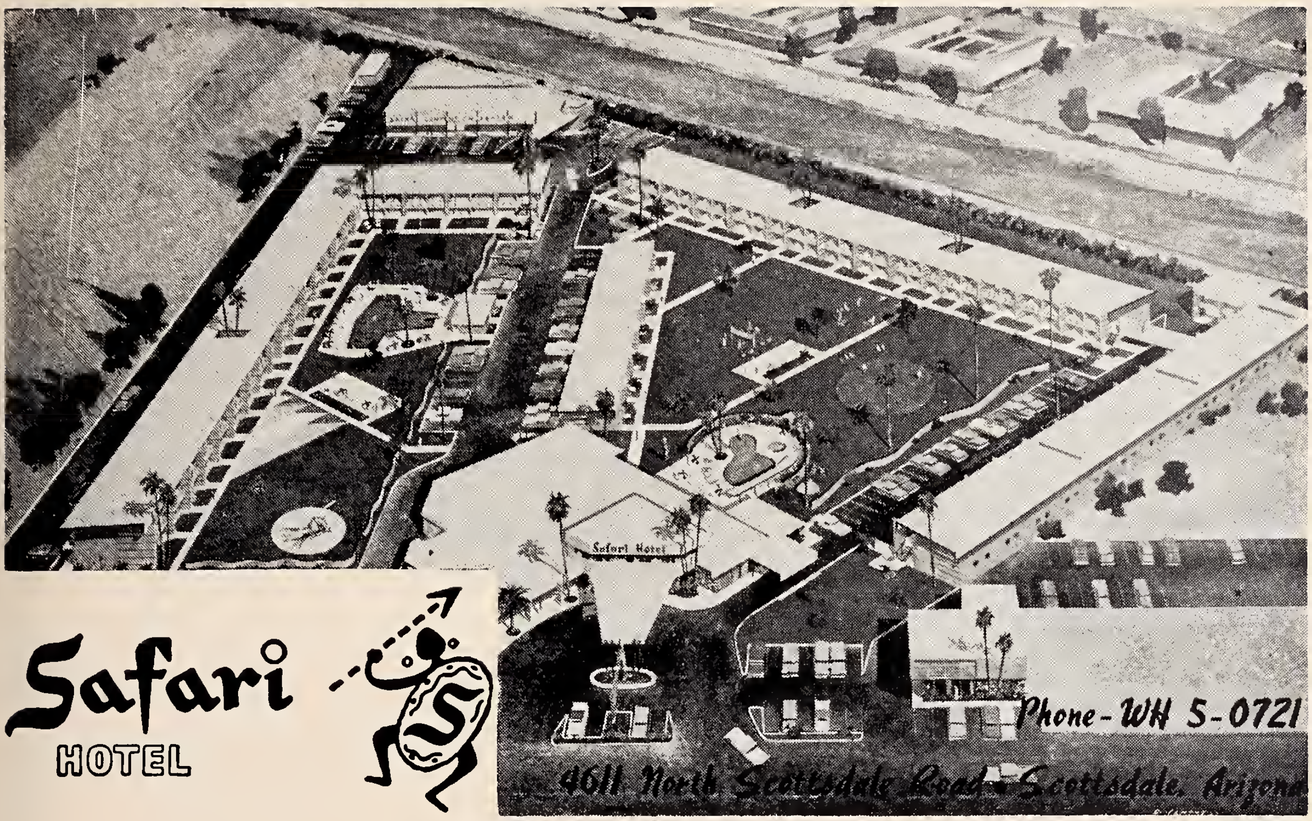
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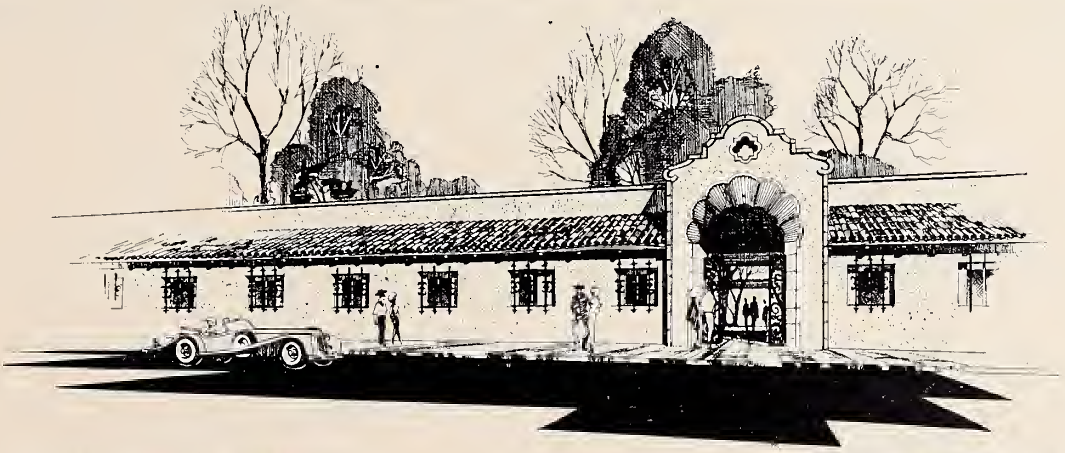

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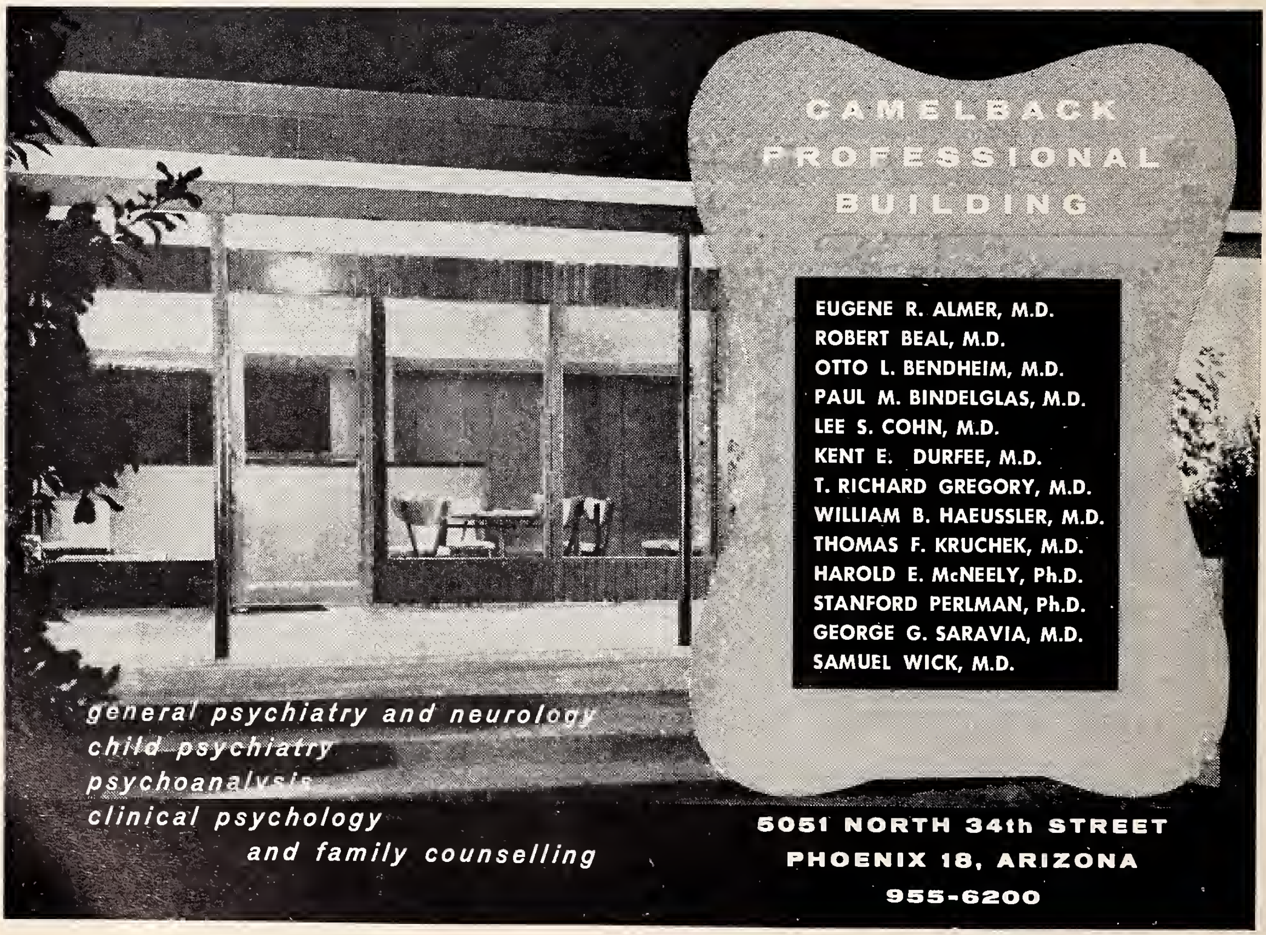

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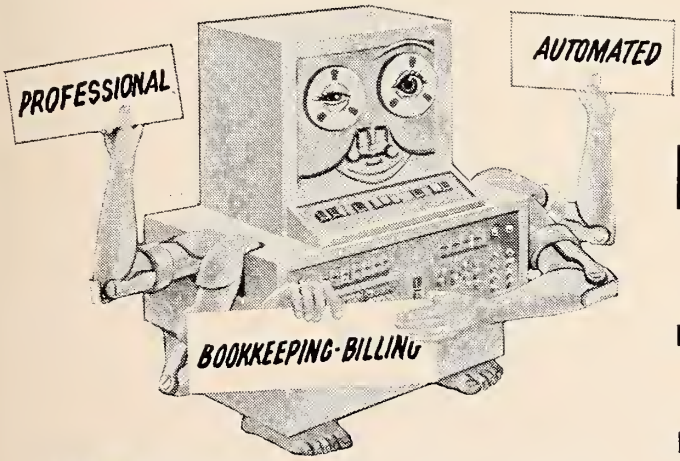

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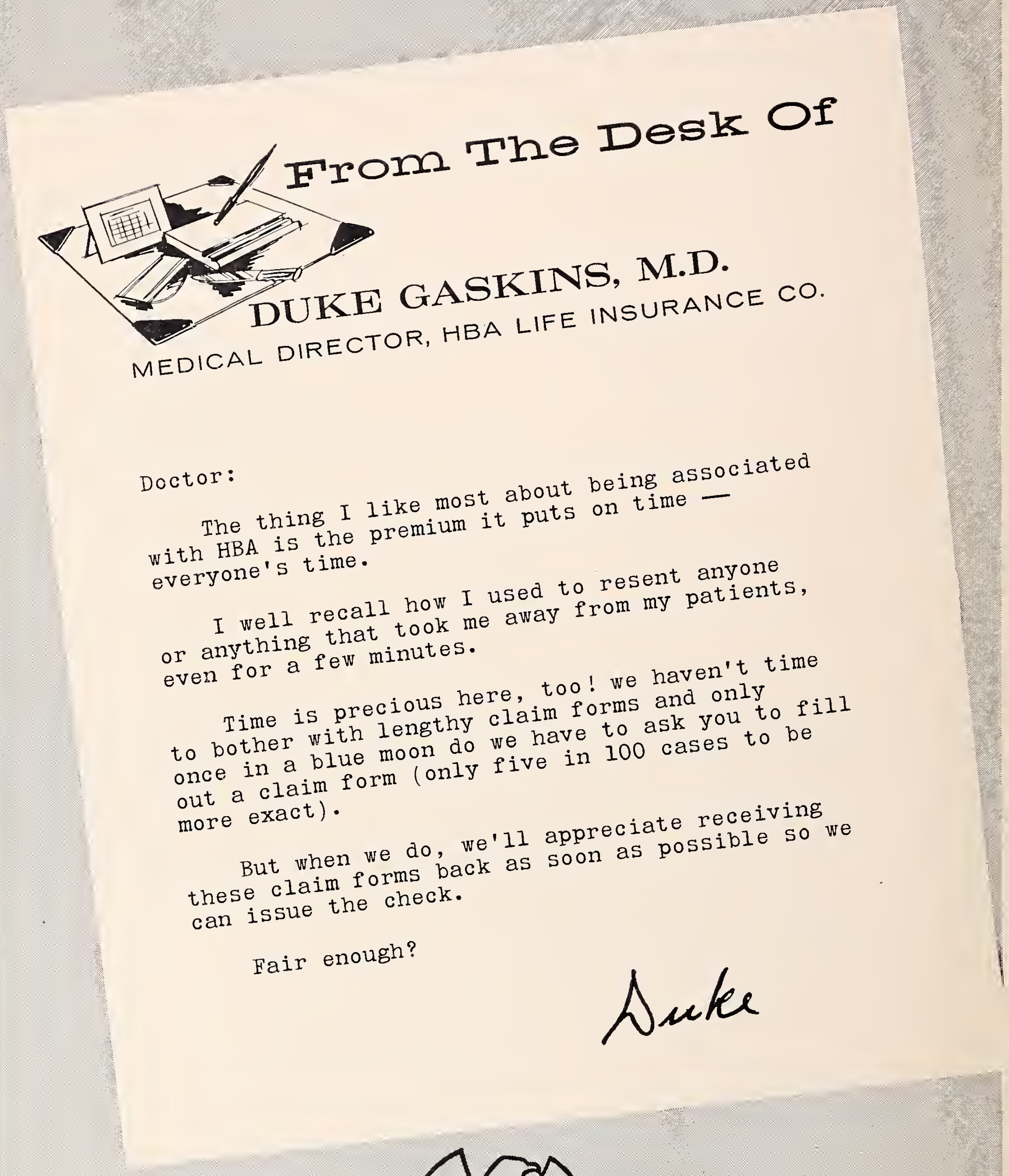

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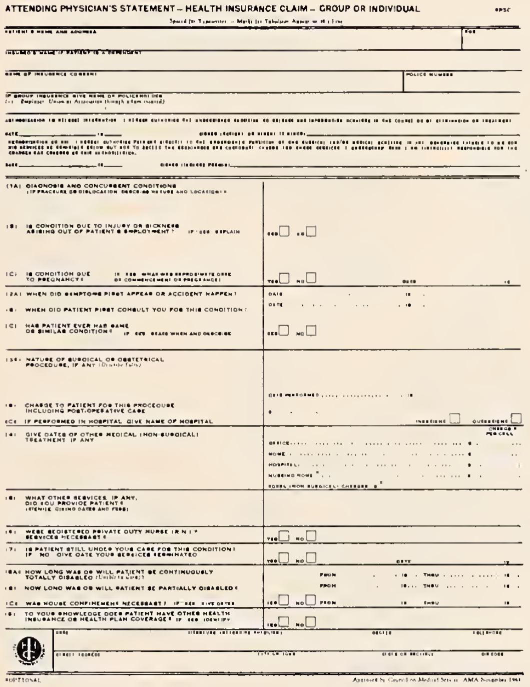

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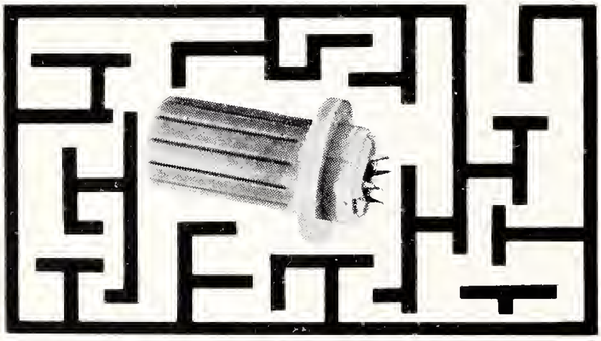

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(Rosenthal)

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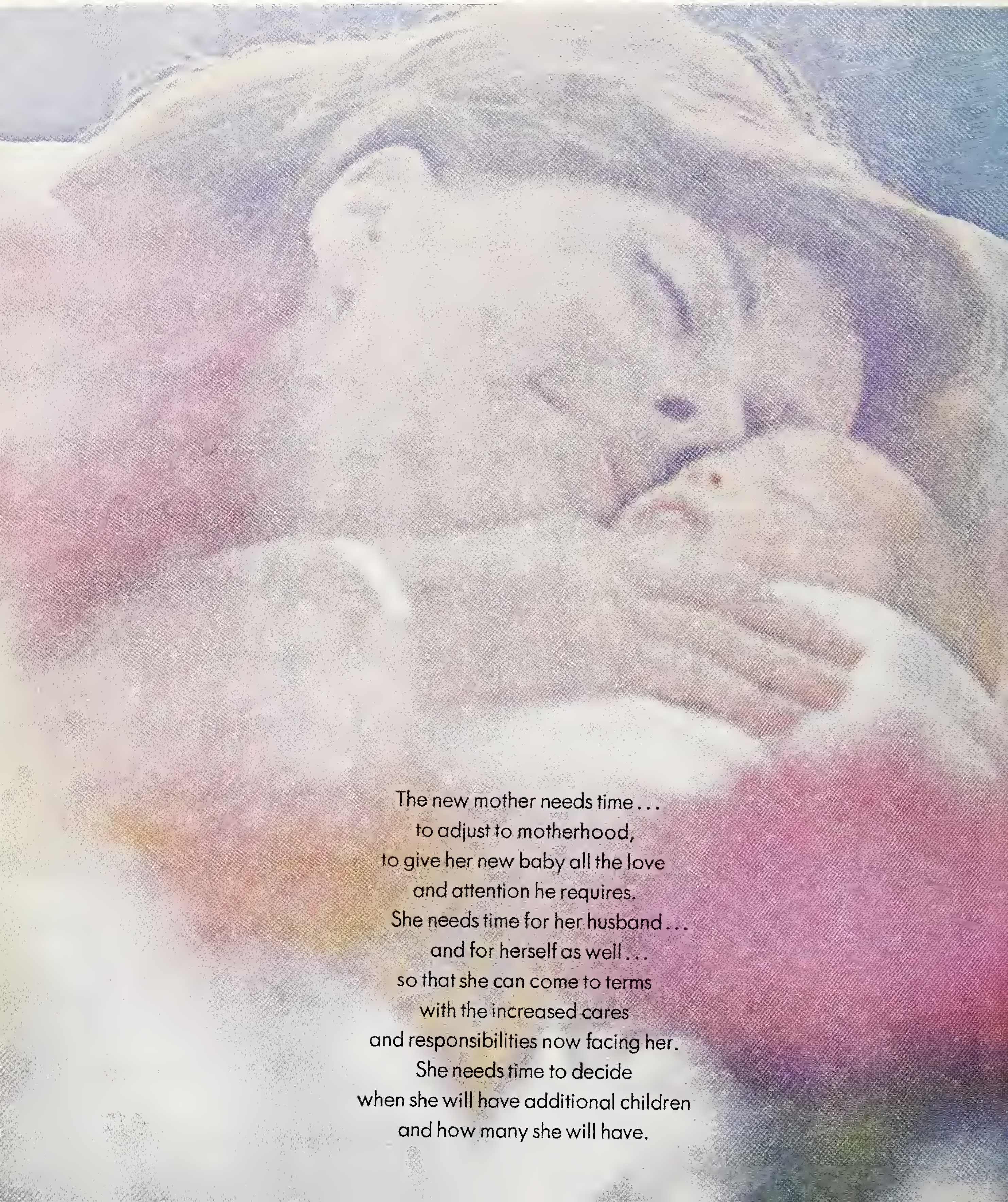
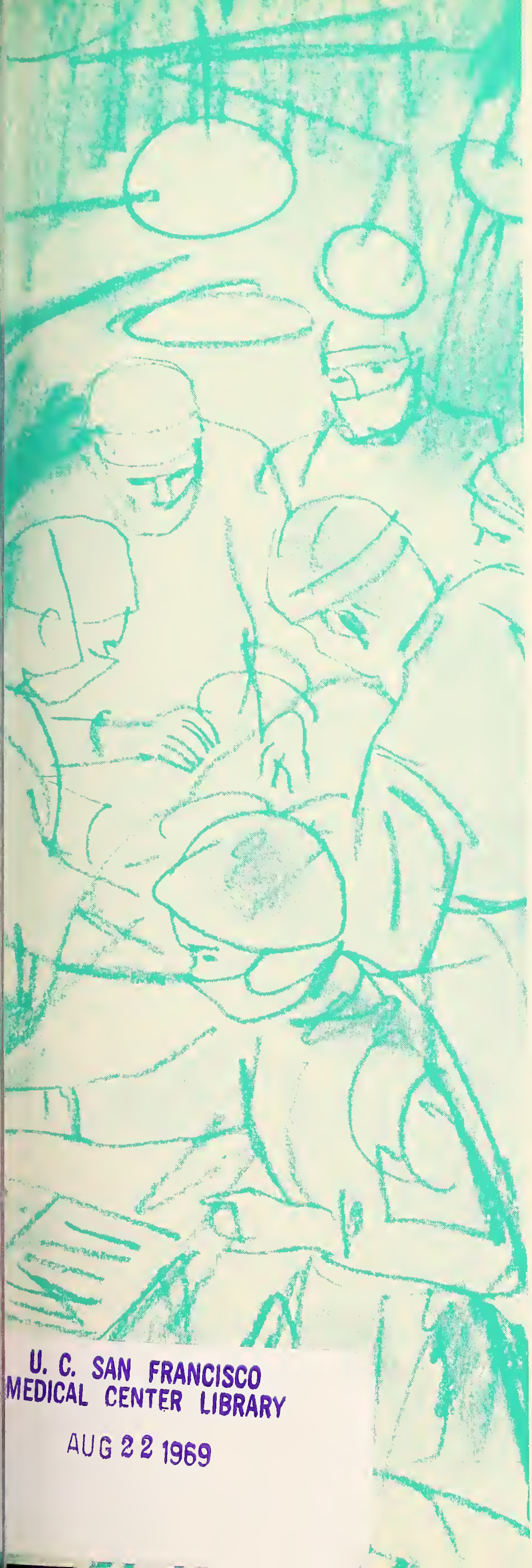
Each tablet contains ethynodiol diacetate 1 mg., mestranol 0.1 mg.



The new mother needs time...
to adjust to motherhood,
to give her new baby all the love
and attention he requires.
She needs time for her husband...
and for herself as well...
so that she can come to terms
with the increased cares
and responsibilities now facing her.
She needs time to decide
when she will have additional children
and how many she will have.



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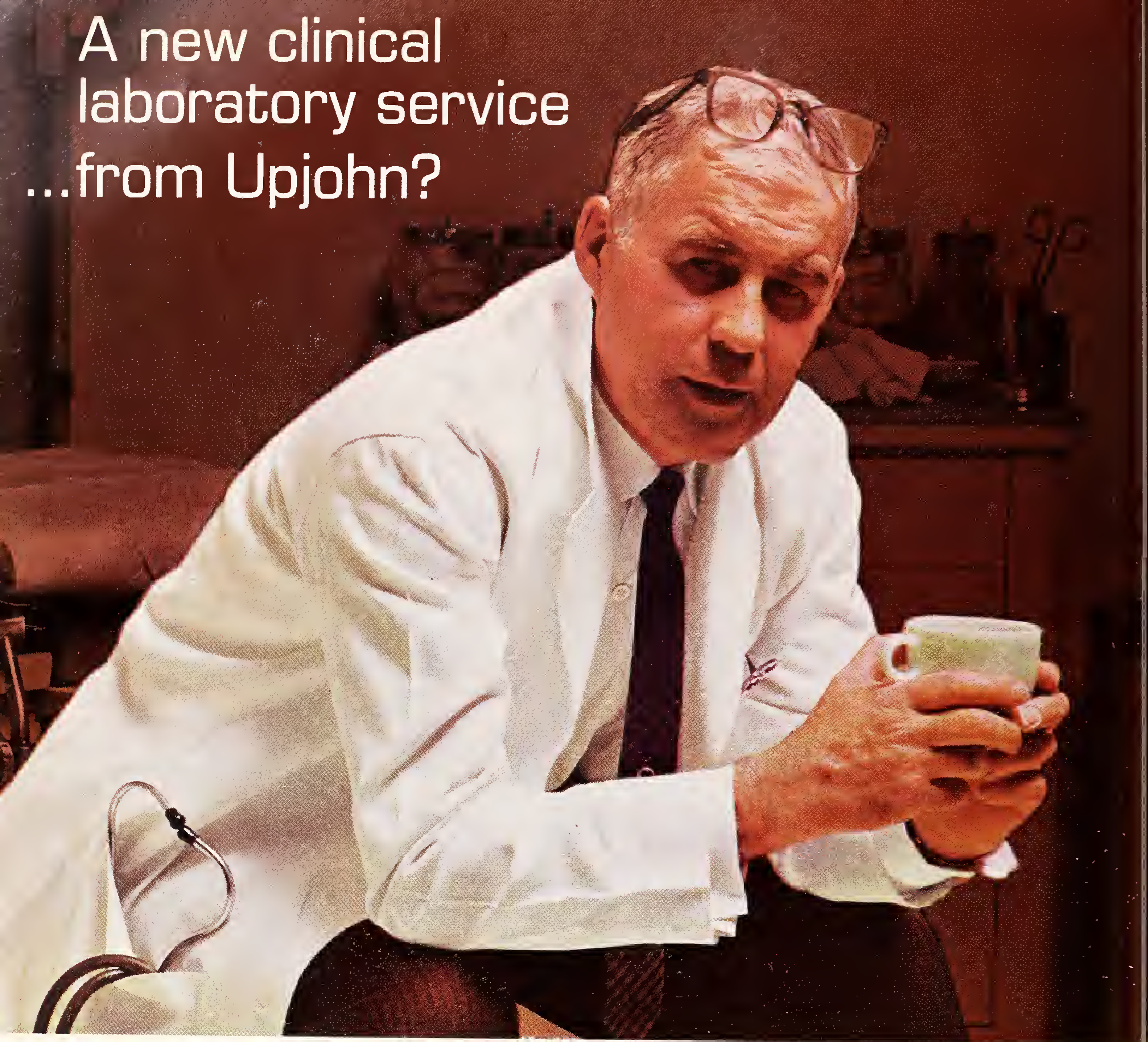
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■ LUTREXIN, the non-steroid "uterine relaxing factor" has been found to be useful by many clinicians in controlling abnormal uterine activity.

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everyday situational stress

When stress is situational—environmental pressure, worry over illness—the treatment often calls for an anxiety-allaying agent which has a prompt and predictable calming action and is remarkably well tolerated. BUTISOL SODIUM (sodium butabarbital) meets this therapeutic need.

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Precautions: Exercise caution in moderate to severe hepatic disease. Elderly or debilitated patients may react with marked excitement or depression.

Adverse Reactions: Drowsiness at daytime sedative dose levels, skin rashes, "hangover" and systemic disturbances are seldom seen.

Warning: May be habit forming.

Usual Adult Dosage: As a daytime sedative, 15 mg. (¼ gr.) to 30 mg. (½ gr.) t.i.d. or q.i.d.

Available for daytime sedation: Tablets, 15 mg. (¼ gr.), 30 mg. (½ gr.); Elixir, 30 mg. per 5 cc. (alcohol 7%).
BUTICAPS® [Capsules BUTISOL SODIUM (sodium butabarbital)] 15 mg. (¼ gr.), 30 mg. (½ gr.).

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AUGUST, 1969/VOL. 26, NO. 8

ARIZONA MEDICINE

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This surgery scene should direct your attention to our lead article appearing on page 651

Published monthly by The Arizona Medical Association, Inc., with offices at 4601 N. Scottsdale Rd., Suite 201, Scottsdale, Arizona 85251. Subscription $5 a year, single copy 50 cents. Second class postage paid at Scottsdale, Arizona, and at additional mailing offices.

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Convalescing . . . but still a long way to go. Anxiety can make it even longer.

Convalescence following medical or surgical procedures may be almost endless to an anxious patient. And, indeed, anxiety with some patients actually retards progress—for example, by inducing insomnia and reducing cooperation.

As physicians have found during nearly 15 years of widespread use, Equanil may be a beneficial part of aftercare. It helps relieve anxiety and tension, thus often aiding your primary therapy.

Indications: For use in management of anxiety and tension occurring alone or as accompanying symptom complex to medical and surgical disorders and procedures. Though not a hypnotic, fosters normal sleep through antianxiety and related muscle-relaxant properties.
Contraindications: History of sensitivity to meprobamate.
Important Precautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.
Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.
Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.
Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.
Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.
Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. (All tablets also available in REDIPAK® [strip pack], Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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(meprobamate)

Wyeth®

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OF SERPENTS AND THINGS

Medical symbolism based on the caduceus or winged staff of Mercury on the one hand, and the staff of Aesculapius on the other, has often exhibited a confusion of historical origin, nomenclature, and perhaps propriety.

The caduceus has been used as a symbol of the medical profession in this country since it was officially adopted in 1902 as the emblem of the U.S. Army Medical Corps. The design consists of the staff of Mercury (Hermes) with two intertwined serpents. Mercury was not only the messenger of the gods but also the god of elegance, trade, skill, the provider of roads, and the bestower of prosperity, as well as being the god of thieves. One story of the origin of the symbol relates that Mercury struck two fighting snakes with a staff and they were pacified. Another story says that the snakes originally appeared as olive branches.

The symbol of the staff of Aesculapius, the Roman god of medicine and healing, with its single serpent entwined, is however, the more appropriate emblem for our profession. The staff may represent a walking stick suggesting the physician's perambulations as he visits his patients. The knots on the staff have been said to indicate the knotty and difficult problems of the physician.

The use of the staff by physicians dates to Susruta who, in specifying roles of dress to his students, included carrying a walking stick. In the Bible the staff symbolizes healing and early Greek physicians carried walking sticks. Ancient statues of Aesculapius show him holding a staff, in some cases encircled with a serpent.

The snake has long been associated with the healing arts symbolizing wisdom, rejuvenescence, longevity, and convalescence. One story tells of Aesculapius treating a patient when Glaucus, a snake, entered and twined about his staff conferring on him the gift of wisdom. The origin of the serpent's healing virtues could relate to the ancient snake worshippers of India. Cretan goddesses of 4000 B.C. have been excavated grasping serpents, and snakes have been considered symbolic of healing since they slough off their skin periodically.

Although the caduceus or staff of Mercury, with its two serpents may look a bit more symmetrical to the designer of plaques or book plates, the gnarled staff of Aesculapius with its single serpent seems both by history and tradition a more proper symbol of the physician.

When it's more than a bad cold

your patient can feel better while he's getting better

Achrocidin®

Tetracycline HCl—Antihistamine—Analgesic Compound

Each tablet contains: ACHROMYCIN® Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Caffeine 30 mg.; Salicylamide 150 mg.; Chlorothen citrate 25 mg.

In tetracycline-sensitive bacterial infection complicating respiratory allergy, ACHROCIDIN brings the treatment together in a single prescription—prompt relief of headache and congestion together with effective control of the organisms frequently responsible for complications leading to prolonged disability in the susceptible patient.

For children and elderly patients you may prefer caffeine-free ACHROCIDIN Syrup. Each 5 cc contains: ACHROMYCIN (Tetracycline) equivalent to Tetracycline HCl 125 mg.; Phenacetin 120 mg.; Salicylamide 150 mg.; Ascorbic Acid (C) 25 mg.; Pyrilamine Maleate 15 mg.

Contraindications: Hypersensitivity to any component.

Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.

Precautions: Drowsiness, anorexia, slight gastric distress can occur. In excessive drowsiness, consider longer dosage intervals. Persons on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity* reactions—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

Upon adverse reaction, stop medication and treat appropriately.

Lederle

348-8

Because any
rologic infection
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for the
strong start
and a
fast finish...

"...a significant gap appears to have been closed in the armory of drugs available to the urologist."[1]
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Cybis® (nalidixic acid) provides prompt broad gram-negative bactericidal activity at normal urinary pH range that can eradicate troublesome *E. coli,* Aerobacter and Proteus. A good starting drug, it can effectively accelerate management of infection due to sensitive organisms.

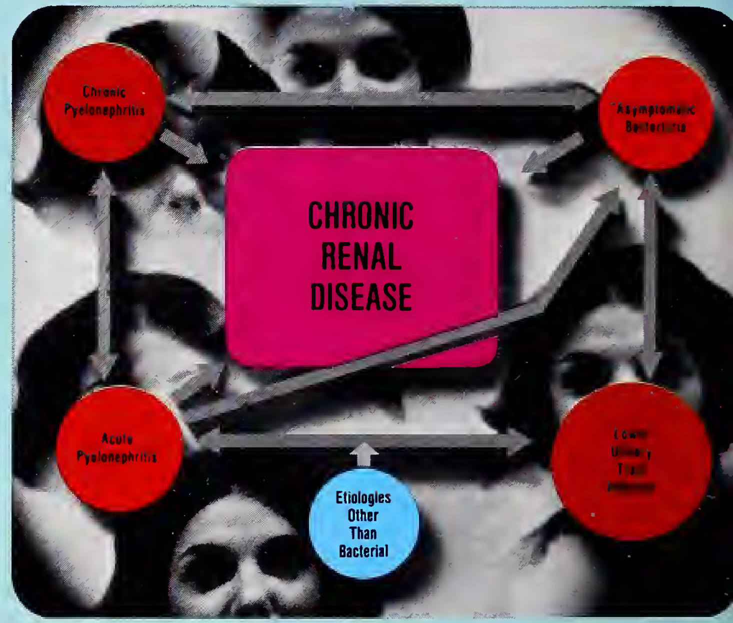
essential control within the primary 72-hour cycle

In cases of acute infection due to susceptible organisms, Cybis works well toward the rapid clearing of disease when obstruction is absent or can be relieved. Within 48 to 72 hours, symptoms are frequently eased and bacteriuria eliminated. Susceptible infection is often eradicated in 10 to 14 days.

blocks the young female progression of infection

Cybis can be useful in naturally susceptible young female patients with new or well-established urinary disturbances. Combining rapid potency with relative freedom of serious side reactions and toxicity, the drug can be of particular value in preventing higher tract involvement or blocking the possible continuum of disease. (See Chart)

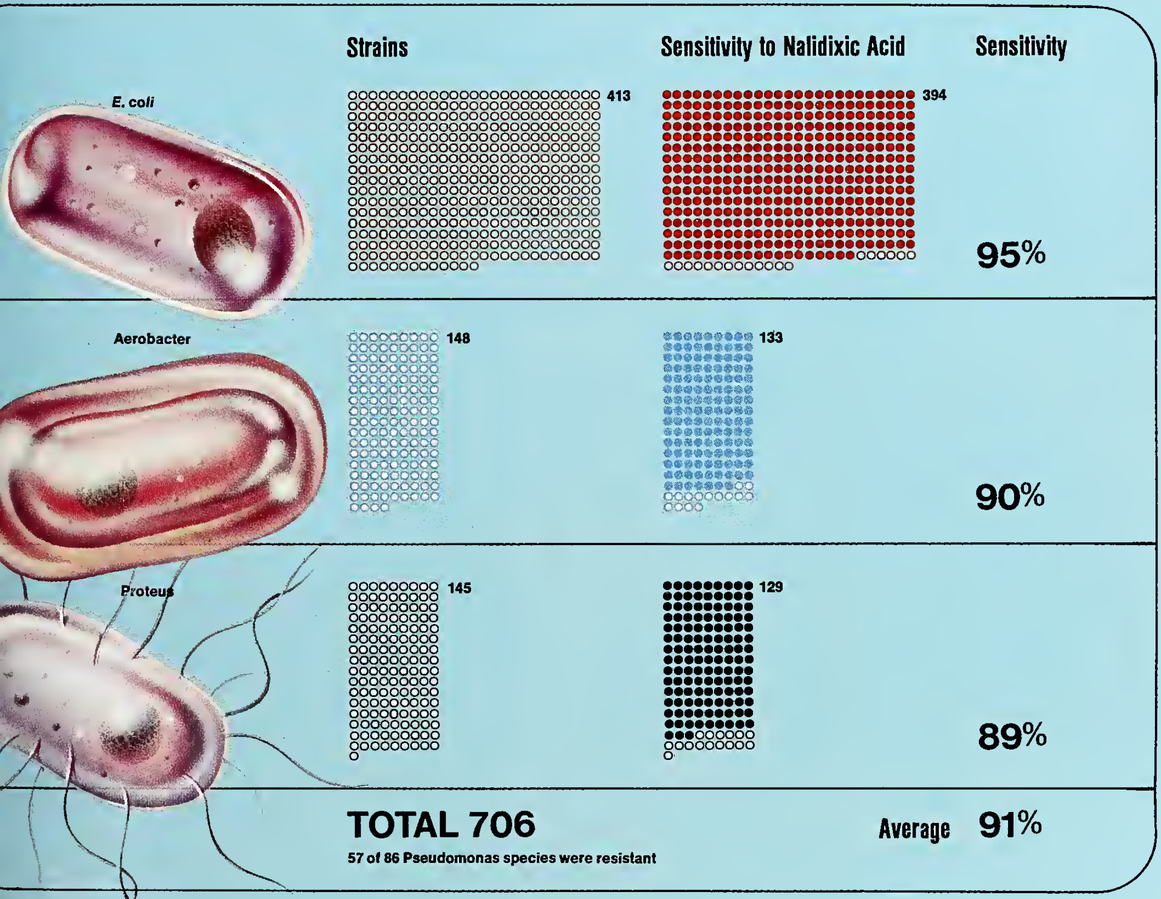
Kinetic Relationship of Acute an Chronic Bacterial Pyelonephritis to Chronic Renal Disease[2]



onsistent activity gainst 706 ram-negative strains

vitro testing of *E. coli,* Aerobacter
d Proteus species showed better
an 90% sensitivity to nalidixic acid.[3]
ee Table)

tter Than 90% Sensitivity Among 3 Common Urinary Invaders



	Strains	Sensitivity to Nalidixic Acid	Sensitivity
E. coli	413	394	95%
Aerobacter	148	133	90%
Proteus	145	129	89%
TOTAL 706		Average	91%

57 of 86 Pseudomonas species were resistant

References: 1. Reimann-Hunziker, R. and Reimann-Hunziker, G. J.: *Praxis* *53*:15, Jan. 9, 1964. 2. Sanford, J. P.: *Med. Times* *96*:715, July 1968. 3. Reese, L.: *Canad. M. A. J.* *92*:394-397, Feb. 20, 1965.

ybis®
(nalidixic acid)

the strong start and a fast finish... in cystitis, pyelonephritis, prostatitis, urethritis

Before prescribing, please consult complete product information,
a summary of which follows on the next page, including indications,
warning, precautions, adverse reactions and dosage.

Summary of prescribing information

Indications: Urinary tract infections in which species of sensitive gram-negative bacteria are predominant, particularly *Proteus, Escherichia coli, Aerobacter, Klebsiella,* and certain strains of *Pseudomonas.* Gram-positive bacteria are less sensitive to Cybis but favorable clinical results have been observed.

Warning: Use in Pregnancy. This drug is not recommended in the first trimester of pregnancy. However, it has been used in several patients during the last two trimesters without producing apparent ill effects in either mother or fetus.

Precautions: Although prolonged treatment with Cybis has been generally well tolerated, as with all new drugs it is advisable to carry out blood, renal, and liver function tests periodically if treatment is continued for more than one or two weeks. The dosage recommended for adults and children should not be arbitrarily doubled unless under the careful supervision of a physician. **It should be used with caution in patients with liver disease, epilepsy, or severe cerebral arteriosclerosis, and in patients in whom kidney function is severely impaired.** Patients should be cautioned to avoid unnecessary exposure to direct sunlight while receiving Cybis and, if a photosensitivity reaction occurs, therapy should be discontinued.

During treatment microorganisms may develop resistance to this drug. Resistant bacteria, not previously present or identified, may emerge. Cultures should be taken and bacterial sensitivity tests made periodically, particularly if the clinical response is unsatisfactory or if a relapse occurs. Should resistance develop, other specific chemotherapy should be instituted; no cross resistance has been observed. If new strains of bacteria that are not sensitive emerge, other effective antibacterial agents may be added. When Benedict's or Fehling's solutions or Clinitest® Reagent Tablets are used to test the urine of patients taking Cybis, a false-positive reaction for glucose may be obtained due to the liberation of glucuronic acid from the metabolites excreted. However, a colorimetric test for glucose based on an enzyme reaction (using, for example, Clinistix® Reagent Strips or Tes-Tape®) does not give a false-positive reaction to Cybis glucuronide.

Adverse reactions: Mainly mild nausea, vomiting, and other gastrointestinal disturbances: less frequently, sleepiness, drowsiness, weakness, headache, dizziness and vertigo, and rarely cholestasis, paresthesia, thrombocytopenia, leukopenia, or hemolytic anemia which in some patients may have been associated with deficiency in activity of glucose-6-phosphate dehydrogenase. Itching, pruritus, rash, urticaria, mild eosinophilia, reversible photosensitivity reactions primarily involving exposed surfaces, and reversible subjective visual disturbances (overbrightness of lights, change in visual color perception, difficulty in focusing, decrease in visual acuity and double vision), occurred occasionally. Reversible increased intracranial pressure with bulging anterior fontanel, papilledema, and headache have been observed occasionally in infants and children. Toxic psychosis and brief convulsions (the latter generally in patients with possible predisp
factors, and both usually associated with excessi
dosage) have been recorded in rare instances.

Dosage and administration: ***Adults*—Four Gm**
by mouth (2 tablets of 500 mg. four times daily) f
to two weeks. Thereafter, if prolonged treatment
indicated, the dosage may be reduced to two Gm
(1 tablet of 500 mg. four times daily). ***Children*—**
According to age and weight: approximately 25
***per pound* of body weight per day, administered**
divided doses.

Note: The dosage recommended above for adult
children should not arbitrarily be doubled unless
the careful supervision of a physician. Until furth
experience is gained, infants under 1 month shou
be treated with the drug.

How supplied: Tablets of 500 mg., bottles of 50.

Before prescribing, please refer to complete prescribing information.

Cybis®

(nalidixic acid)

for the strong start and a fast finish...
in cystitis
pyelonephritis
prostatitis
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introducing an anticostive* antacid

*Avoids constipation.

Gelusil-M avoids constipation

- Gelusil-M has been formulated to help avoid constipation in these patients: hospitalized/bedridden/debilitated/sedentary/pregnant/elderly/on a bland diet/on anticholinergic-antispasmodic drugs/when straining at stool should be avoided.
- Magnesium content helps maintain intestinal fluid volume and motility.
- Some patients may develop loose stools while taking Gelusil-M. This condition is usually dose-related, and usually responds to dose reduction.

introducing

GELUSIL®-M NEW

each 5 ml. teaspoonful contains:
500 mg. magnesium trisilicate
250 mg. aluminum hydroxide (Warner-Chilcott)
200 mg. magnesium hydroxide
*U.S. Patent No. 3,326,755

a consistent buffering anticostive† antacid

†Avoids constipation.

See next page for prescribing information ▶

GELUSIL–one name to remember...and a dosage form for every patien

Gelusil®-M Liquid

Indications: Gelusil-M is indicated for prompt and dependable symptomatic relief of peptic ulcer, gastritis, heartburn, hiatal hernia, esophagitis, and other conditions for which control of gastric hyperacidity is required.

Precaution: Prolonged or intensive therapy in patients with severe renal insufficiency may lead to hypermagnesemia.

Dosage: One to two teaspoonfuls (5 ml. to 10 ml.) between meals and at bedtime or whenever symptoms occur. Certain conditions, such as acute peptic ulcer, may require individualized dosage. If diarrhea occurs, reduce dosage or discontinue use.

Supplied: Gelusil-M (spearmint-flavored)—light green bottles of 12 fl. oz.; and a **special hospital pack.** Keep tightly closed—shake vigorously.

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Easy to take along / easy to take / pleasantly mint-flavored. An antacid with adsorbent and demulcent properties which contains in one tablet: 0.25 Gm. aluminum hydroxide (Warner-Chilcott) and 0.5 Gm. magnesium trisilicate (USP).

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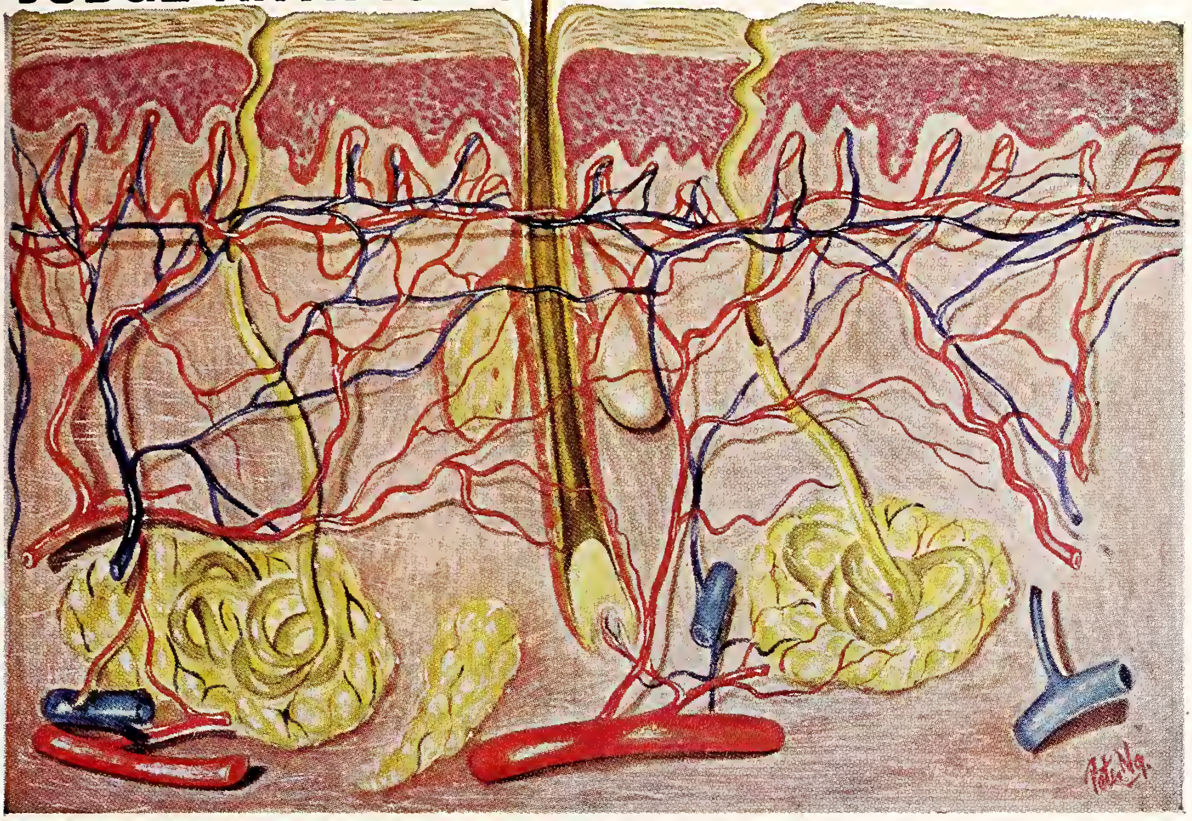

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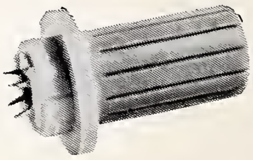

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Circulating Manager .... Mrs. T. Herman Moore (Teddy)
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SAFETY-DISASTER PREPAREDNESS:
Mrs. Charles I. Fisher (Peggy)
352 West Berridge Lane, Phoenix 85013

WA-SAMA .... Mrs. Ruben Acosta (Mary)
3481 E. Edgemont, Tucson 85716

ArMA Reports

THE MINUTES APPEARING IN THIS SECTION HAVE BEEN EDITED TO CONSERVE SPACE. A COMPLETE COPY OF THE MINUTES OF ANY MEETING WILL BE MAILED TO ANY MEMBER REQUESTING THEM.

MEDICAL ECONOMICS COMMITTEE

Meeting of the Medical Economics Committee of the Arizona Medical Association, Inc., held Sunday, June 29, 1969, in the Central Office of the Association, Suite 201, Safari Building, 4601 North Scottsdale Road, Scottsdale, Arizona convened at 10:10 A.M., Harvey G. Brown, M.D., Chairman, presiding.

ICA INSURANCE CLAIM FORMS

Because of the mounting objections received from physician members handling workmen's compensation cases as to distribution of the new ICA insurance forms required forwarded to the employer, the insurance carrier, and others, it has been suggested desirable that effort by this Committee be undertaken to convince ICA that such distribution be made by it. Frequently, the injured employee does not even know his employer, having been employed by a foreman, and does not know the name of the insurance carrier. Certainly, the physician has not this information.

George W. King, M.D. (Tucson) by letter dated January 15, 1969, addressed to the Pima County Medical Society, points up the previous comments based upon his experience, and comments further upon the additional clerical work necessitated because of the claim form revision. He requests that vigorous protest of the added requirements, previously assumed by ICA, be made and insist that the Commission accept the burden of assembling these medically extraneous data or increase its fee for initial industrial visit. The Society Board of Directors refers this matter to the Medical Economics Committee of ArMA in the hope the situation might be alleviated in the near future.

Dr. Edwards refers to paragraph D of the statute § 23-908 — injury reports by employer and physician; fees of physician; violations; penalty — which reads as follows:

> "D. When an accident occurs to an employee, the employee shall forthwith report the accident and the injury resulting therefrom to the employer, and any physician employed by the injured employee shall forthwith report the accident and the injury resulting therefrom to the employer, the insurance carrier and to the commission."

Paragarph G reads as follows:

> "G. Immediately upon notice to the employer of an accident resulting in an injury to an employee, the employer shall provide the employee with the name and address of the employer's insurance carrier, the policy number, and expiration date."

Dr. Edwards further stated that the injured employee should be in position to inform the physician as regards the employer and insurance carrier. The employer is required to furnish this data in card form to the injured employee. It would be fruitless to appeal to the Commission to modify this statutory requirement. Solution would be to amend the law or encourage the Legislature to be more generous in its appropriations to enable the Commission to assume this additional detail as before. The problem is the inability of ICA to perform this function under current budget limitations.

Dr. Chesser advised this subject has been discussed locally with Senator Holsclaw and it is the hope a suitable amendment will be introduced during the next legislative session.

It was the consensus that this subject should be included for discussion when next conferring with the Industrial Commission of Arizona; also, the Legislative Committee of this Association should be apprised of the situation and encouraged to support or have introduced an appropriate amendment to the statute.

AMA RESOLUTION NO. 48 (C-68)

Substitute Resolution No. 48, adopted, as amended, by the House of Delegates of the American Medical Association in Clinical Convention — 1968, prescribed definitions of the terms usual, customary and reasonable, as relates to physicians fees and recited below:

> "WHEREAS, There is a rapidly increasing number of programs for financing health services based upon the **usual, customary** and **reasonable** concept for payment of physicians' services; and
>
> WHEREAS, It is in the best interest of the public and physicians of the country that a national definition of the terms **usual, customary** and **reasonable** be formulated by the American Medical Association; therefore be it
>
> RESOLVED, That the American Medical Association adopt the following definitions and distribute them to all state medical associations for their individual consideration and guidance:
>
> > **Usual** is defined as the "usual" fee which is charged for a given service by an individual physician in his personal practice (i.e., **his own usual fee**);
> >
> > **Customary** is defined as the range of usual fees charged by physicians of similar training and experience for the same service within a given specific limited geographic or socio-economic area;
> >
> > **Reasonable** is defined as a fee which meets the above two criteria, or, in the opinion of the responsible local medical association's review committee, is justifiable in the special circumstances of the particular case in question; and be it further
> >
> > RESOLVED, That whenever these terms are used in contracts or laws that they be specifically defined in those documents."

WORKMEN'S COMPENSATION CHAPTER 6, LAWS OF 1968

It was voted that this Committee previously had requested a hearing before the Industrial Commission of Arizona, as newly constituted, to discuss matters relating to industrial cases; further, that the Commission sought deferment of from three to six months to allow the ICA to organize in its new capacity. The period of postponement has now expired. To expedite compilation of facts by ICA for discussion when the hearing is held, ArMA is requested to forward any information or pertinent facts assembled to substantiate any proposal it may be intending to place before the Commission.

The Board of Directors of this Association in meeting held July 14, 1968, directed this Committee to proceed to negotiate further with ICA as regards adjustment of the existing fee schedule in line with the usual, customary and reasonable fee concept, the new statute providing for annual reevaluation of the fee schedule. It was suggested a survey be undertaken among those doctors doing the bulk of workmen's compensation work seeking information and data regarding charges; their attitude toward fees currently being paid; also, their philosophy as regards working under a fee schedule. Dr. Edwards, Medical Director, State Compensation Fund, under date of March 24, 1969, at the request of this Committee, has furnished a listing of doctors who in 1968 received an income of $4,000.00 or more handling a large proportion of workmen's compensation cases.

It was the consensus that the Committee proceed and expedite the survey proposed, the chairman to direct the promulgation of questions to be asked in order that the results will be meaningful; and that we categorize our problems to be presented before the Commission fortifying them with the results of the proposed survey, to include previous complaints regarding (ICA) Rule 59-A and those currently being received relating to the newly devised claim form distribution procedure.

Attention was directed to the availability this Fall of the Fifth Edition — 1970 Relative Value Studies adopted by Council of the California Medical Association, May 10, 1969, to be implemented April 1, 1970. Copies will be available through CMA at $15.00 each. CMA appeared before the Administrative Director, Division of Industrial Accidents (California) petitioning that the coefficient fee level incorporated under the 1966 Workmen's Compensation official Minimum Medical Fee Schedule be increased from the present $5.50 per visit to $6.50 per visit, such increase to become effective October 1, 1969.

KEOGH PROTOTYPE PLANS

Valley National Bank Proposal

Mr. Roman G. Mislicky, Assistant Vice President, Manager of Professional Services Division, Valley National Bank, and Mr. Kelsey L. Moline, Manager of Employee Benefits Division — VNB, on invitation, appeared before the Committee presenting a self-employed retirement program. Mr. Moline outlined the details as follows:

Type of Plan

Each employment unit whether a partnership, proprietorship or individual, will have a separate plan and Trust agreement. The basic provisions of the agreement will be standardized. Options will be available to allow each employment unit to select terms to fit its own special requirements. This plan will not be what is generally called a "master plan" where all employing units become attached to one plan and Trust. This plan will be a standardized prototype plan that each employing unit can execute as its own with its modifications included as part of the one document.

Investment Program

For each Trust the bank would prefer to be given full control over investments. This gives the greatest flexibility to the investment program because the investment skills of the bank can then be used on a day to day basis for the maximum benefit to the particular Trust account.

Recognizing that some employment units may wish to have a measure of control in this important aspect of the retirement program, the available plan will provide the opportunity to determine investment policy by selecting investment classifications as a guide to the Trustee.

A portion of the contributions to the plan may be alloted to a life insurance account to be used for the purchase of life insurance, endorsement or annuity contracts.

Contributions

The employing unit will be able to select the measurement formula desired in determining the rate of contributions. This will include elections generally referred to as "the profit sharing approach" or as "the pension plan approach".

Availability

The program should be ready for use in the ealendar year of 1969. Our target date is October 1, 1969, which leaves the entire 4th quarter for the enrollment of cashbasis taxpayers.

Cost

The tentative schedule of the bank's charges will include an initial set up charge of $50.00. Annual charges will be at the regular trust rate of $6.00 per thousand of assets held in the Trust. Since these Trusts will be small at the outset, the regular minimum annual charge of $200.00 will be suspended for the first six years of operation of each Trust. Instead a minimum annual charge of $75.00 will be applicable to the first three year period and $125.00 will be applied for the second three year period.

Maintenance of accounts for individual participants can also be arranged with the bank at its normal rates for this service.

Mr. Moline advised the proposal is before the Internal Revenue Service for review and approval which is expected by October 1, 1969.

Considerable discussion ensued and Mr. Moline responded to many questions propounded. On the basis of national experience, Court decisions, and possible future legislative enactments, VNB will place emphasis on the Professional Corporation business rather than the Keogh Plan.

It was determined to recommend to the Board of Directors approval of this VNB proposal for consideration of the membership.

ArMA Keogh Plan

Mr. Charles Fisher, President, Armada Assurance Agency, Inc., proposes the creation by ArMA if its own H.R. 10 Plan, he to serve as Administrator. His comments are as follows:

"After three years of study, work, and experience with H.R.-10 plans and individuals participating in such plans, the following conclusions are presented to support this recommendation.

1. The average self-employed individual or professional man entering into a Keogh contract in the main is at the mercy of some individual. This individual might be an insurance agent, a securities representative, or a trust officer, each representing just one approach to H.R.-10, each having his own company's or bank's respective H.R.-10 prototype or master plan.

2. H.R.-10 participants might also be at the mercy of an agency such as the Armada Agency and subjected to undesirable changes within a plan by the trust department of a bank. This has been true in the "Armada Plan" even though this plan was designed and put together very carefully and in close association with the Trust Division of the Guaranty Bank, now United Bank of Arizona. Such changes have come about largely as a result of personnel replacement at the top echelon. The Trust Department's attitude and approach to H.R.-10 is much different from our original concept. The relatively unlimited investment directions and flexibility originally enjoyed are becoming undesirably restrictive.

3. Most individuals presenting a Keogh plan of one sort or another lack a complete overall and detailed knowledge of Keogh or H.R.-10. The insurance agent sells his company's plan. The N.A.S.D. or fund representative sells a fund and its prototype. The trust officer sells his bank and its master plan. Each person has one purpose: make a sale, whether the sale fits the need or not.

Lack of knowledge results from (a) insufficient time to concentrate on H.R.-10; (b) the necessity of making one's living selling products somewhat removed from those involved in H.R.-10. These selfsame people are not familiar with the requirements of follow-through. They do not keep individual account records for owner-employees. In fact there are no provisions for this service in the A.M.A. or the A.A.G.P. or the New England States plans. None of these plans will advise a doctor when he has an employee becoming eligible. None of these plans will inquire as to wage increases which would cause a change in employee deposits. In most cases, as it is spelled out in the A.A.G.P. plan, the doctor is expected to administer his own plan.

4. It appears with the size of the Arizona Medical Association and the number of its members participating in H.R.-10 and those who will be participating, or will be incorporating, that these members should share their experiences and knowledge and have one focal point of information which can be thoroughly relied upon. The membership could benefit from a special knowledgeable and permanent committee being formed to select and recommend to the Board of Directors and the membership an agency to serve as administrator in this capacity.

The Association through this committee should be in a position to serve its members by making sure that the administrator provides this information, accounts to the Association for all of its actions and activities and of its business conduct. This committee and the Association would further have the responsibility of selecting a new administrator should it become necessary because of malfeasance or death or other valid reason.

5. We feel that with a hundred or more doctors joined together in a plan, with a singleness of purpose and with the common denominator of profession, there should be a little more control and direction available than is at present.

We feel that the Arizona Medical Association can supply additional and most important services simply by creating its own plan. By so doing it can determine the future of that plan and, above all in our opinion, the most important reason for creating the ArMA plan is that ArMA is a "forever" corporation and is forever here for its members.

6. The administrator, in addition to working with the Association on the H.R.-10 program, can also serve by putting together specialty teams for the professional corporation. It is anticipated that I.R.S. will eventually give up to the advent of the professional corporation. An unbiased service should be available to those members of the Association interested in incorporating. We feel that the administrator, if properly supported, can serve the Association in many ways with its profits and in gratitude for its position.

7. The Association, by creating its own plan and utilizing the services of an administrator, can offer, a plan as broad as permitted by regulation with a maximum of flexibility. The vast amount of work and effort will be absorbed by the administrator.

8. It is important that the Board of Directors, the Executive Committee, and the membership as a whole of the Arizona Medical Association be aware that should the Armada Agency be named as administrator initially in this program, it must constantly and continuously give evidence of integrity in its operation, of complete and honest service in all of its programs or it is subject to being replaced at the will of the association membership."

Discussion ensued. It was determined to recommend this proposal to the Board of Directors for the consideration of the membership following interrogation of Mr. Fisher by the Chairman and presentation of an official proposal.

COMMUNICATIONS

Professional Liability Insurance

Mr. Charles Fisher, President of the Armada Assurance Agency, Inc., proposes offering through Hawaiian Insurance & Guaranty Company, LTD., a deductible ($1000.00 — 25% discount) professional liability ($100,000/$300,000) policy reflecting the following savings (letter of June 20, 1969):

Class	No Deductible	$1000 Deductible (25% Discount)
I	$ 316	$ 237
II	554	416
III	948	711
IV	1264	948
V	1580	1185

The $500 Deductible (15% discount) submitted was withdrawn.

It was the consensus this proposal should be accepted providing certain questions raised ($1,000 deduction per claim or otherwise) is determined satisfactory on interrogation by the Chairman.

Truth-in-Lending Act

Counsel under date of June 18, 1969, submits a memorandum concerning the Truth-in-Lending Act. Referring to Example 2:

> "Dr. X (or his law firm) bills patients (clients) by monthly statements which do not state any terms of payment. Occasionally, a patient (client) is unable to pay the full amount of the bill and the creditor informally agrees to forbear suit so long as the debtor makes reasonable monthly payments in liquidation of the debt."

Counsel states: "You will note that he (Mr. Cohen) concludes the Act is not applicable to doctors because no financing charge is involved, disclosure is required only when applicable, doctors do not regularly extend credit with a financing charge, and when they do extend credit, they do not ordinarily enter into a contractural relationship. Additionally, this is not a regular practice on the part of most physicians."

For the information of the Committee, Mr. Mislicky read the content of letter forwarded to its VNB Medac Service members to assure its interest in assisting their compliance with the Truth-in-Lending Law (Consumer Credit Protection Act). It is stated that doctors generally do not add a service charge to their patients' bills so they assume that they are exempt from the provisions of the new law. However, the law also states that, whether or not an additional charge is imposed, if you arrange for the payment of fee in more than four instalments, you are covered by the law. Needless to say, the Bank is quite involved in this law and its attorney too has been reviewing its ramifications and effect. Three examples were presented wherein a physician may become involved, especially in the field of obstetrics. It is suggested that ArMA counsel might wish to review these situations and comment. It was so ordered.

MEETING ADJOURNED AT 1:30 P.M.

Edward Sattenspiel, M.D.
Secretary

GOVERNMENTAL SERVICES COMMITTEE

Meeting of the Governmental Services Committee of The Arizona Medical Association, Inc., held Thursday, June 5, 1969, in the Directors Room, Safari Hotel, Scottsdale, Arizona, convened at 7:18 P.M., Woodrow W. Scott, M.D., Chairman, presiding.

MINUTES

Minutes of the meeting held March 2, 1969, were approved as distributed.

PART A — INTERMEDIARY ARIZONA BLUE CROSS

ECF Survey

At the meeting of March 2, 1969, Blue Cross was asked to conduct a survey on the following items:

INFORMATION ABOUT ECFs

1. Number of registered nurses per bed
2. Number of licensed practical nurses per bed
3. Number of aids per bed
4. Number of square feet per patient (assuming 100% occupancy)
5. Average length of stay by diagnosis (use the five most common diagnoses)
6. Size of ECF requiring a full-time dietitian
7. Size of ECF requiring a full-time physical therapist
8. Cost of Utilization Review Committee
9. Cost of Medical Records Committee
10. Frequency of M.D. visits
11. Cost of drugs (use the five most commonly prescribed drugs)

INFORMATION ABOUT HOSPITALS

1. Charge per day by diagnosis (use the five most common diagnoses)
2. Cost per day by age
3. Charge per day for intensive care units
4. A statement as to what Blue Cross is doing to help ensure efficient utilization of staff

The following is the report as presented and explained by Mr. Yost.

This report is the result of combined efforts of the Arizona State Department of Health and Arizona Blue Cross.

Items 1, 2, 3, 4, 6 and 7 of the questionnaire were submitted to the State Health Department and this reply is attached without comment.

The answer to question No. 5 is taken from the utilization reports supplied to each provider and Utilization Review Committee Chairman on a quarterly basis. The average length of stay for the five most commonly occurring diagnoses in ECFs is 30.5 days. The overall average length of stay in ECFs is 28.9 days.

The average cost (question No. 8) of having a Utilization Review Committee in an ECF is $181.00 per annum.

We are unable to provide the answer to question No. 9 because we have no figures identifying the cost of Medical Record Committees.

Question No. 10 was referred to Aetna Medicare Claim Administration, resulting in the reply that such information would be available directly to the Governmental Services Committee if so requested.

Concern for frequency of visits has been evidenced by the State Health Department, the providers and by Blue Cross as Intermediary. The Medicare program as well as the satate licensure laws require physicians' visits in ECFs and in licensed nursing homes no less often than every 30 days. It is not uncommon to be advised that patients are not seen after admission for periods extending over a year or more. Hence our concern is that in some, if not many, cases the visits are not frequent enough.

The answer to question No. 11 is not available from current records. To secure information on cost of drugs based on the five most commonly prescribed would require several additional steps in auditing or a comprehensive survey, neither of which are we at present authorized to expend the necessary monies to undertake.

Those questions relative to hospital charges are answered as follows:

1. Average hospital charge per day $70.06. (our records would not permit breakdown by diagnosis)
2. Cost per hospital day averages $62.18. (Unable to

break this down by age group)

3. The average charge for intensive care units is $110.83 per day.
4. This question requires a narrative reply and is applicable to both hospitals and ECFs.

All institutional providers of service are reimbursed on the basis of audited cost. The individual provider's cost report is audited annually and must meet a test of reasonableness. The test for reasonableness is primarily based on a comparison of cost in other institutions providing like services. At the time that the Medicare auditors perform the annual audit, all salary costs are reviewed for reasonableness as well as accuracy. If excessive or unreasonable costs appear, the causes are investigated and recommendations made for the providers in the "management letter" prepared for each audit. When costs are found to be unreasonable, the total amount of reimbursement is reduced to the amount deemed reasonable by the audit team.

Health Department portion:

1. **Number of Registered Nurses per bed** – 1 R.N. to 12.4 beds (Based on a 24-hour day)
2. **Number of Licensed Practical Nurses** – 1LPN to 33.2 beds (Based on a 24-hour day)
3. **Number of Aides per bed** – 1 Aide to 3.8 beds (Based on a 24-hour day)

Items 1, 2, and 3 are based on the total licensed capacity of the ECF as opposed to the number of beds certified under Medicare. The reason for this is because our licensing standards are higher in some respects than Medicare; therefore, the staffing for the distinct part of a facility which is certified would be extremely difficult to figure. The nurse staffing ratios shown also include part-time nurses, but because of the difficulty in accounting for these part-time persons, no attempt to shred these figures out to full-time equivalents was made. However, this does tend to inflate the ratio of nurses to beds. Please note that the above figures are for the entire 24-hour coverage. Therefore, to get the number of persons on duty on any one shift, these figures have to be broken down by eight hour shifts; but to do so evenly (i.e., multiply by 3) would not be accurate because the evening and night shifts routinely have less personnel than day shifts.

It should be noted that the above ratios are for the nursing home-ECF combination and do not include any long-term or ECF beds in hospitals. It should also be noted that, in the larger facilities which employ a Director of Nurses (in addition to charge nurses on each shift), the Directors of Nursing were not included in these ratios.

As to item #4, the current State licensing requirement is 60 square feet per bed in multiple bed rooms and 100 square feet per bed in single rooms. However, the recommended minimum square footage for patient rooms is 80 square feet per patient in multiple occupancy rooms, and a minimum of 100 square feet per room in private rooms. This is not the current Federal minimum for bed space. Please note that this does not take into consideration the space required for bathrooms, storage, recreation, dining, administration, treatment rooms, etc. Since extended care facility patients are, by definition, those who require post-hospital care of a level generally higher than that required of long-term care or domicilliary care patients, the square footage of patient rooms must be sufficient to include that equipment – I.V. stands, orthopedic frames, lifting devices, oxygen equipment, etc. – generally used in the care of acute patients.

Regarding Items #6 and #7, after a study of those facilities which have full-time dietitians and physical therapists, plus the recommendations of the consultants in these areas in our Department and in the Department of Health, Education and Welfare, a set standard for full-time utilization cannot be made due to changing patient load by type of care required and utilization of the specialty within the facility by administrative decision. However, based on all the advice from the various consultants contacted, they believe a well-operated ECF could utilize dietitians and physical therapists on a full-time basis as follows:

Dietition – one hundred beds or larger

Physical Therapist – one hundred beds minimum for full utilization of one physical therapist, with a maximum of 300 beds for one physical therapist with up to six technicians to assist.

PART B — CARRIER
AETNA LIFE & CASUALTY CO.

Fee Freeze

Mr. Blazek reported on the current Medicare freeze on fees as outlined in a recent issue of MEDICAL MEMOS. It was suggested that ArMA members be advised to continue to charge Medicare their current usual and customary fees even though they know that they may be reduced. This is important in order to keep the individual's fee profile on a current basis for the time when the fee freeze is lifted.

Travelers Insurance

Dr. Scott introduced Mr. John Manalo, Supervisor of Medicare for The Travelers Insurance Co. Mr. Manalo explained that his company handles all Medicare work for the Railroad Retirement Board throughout the country. Mr. Manalo has a staff of four and they process approximately 1,800 claims per month.

SECTION ON COMPREHENSIVE HEALTH PLANNING

Dr. Farnsworth reported that the State Health Planning Authority is well under way under the guidance of Melvin Goodwin, Ph.D. The Authority's Advisory Council is in the process of being appointed by the Governor.

CMA Regional Conference

Dr. Farnsworth reported that the California Medical Association is planning a second regional conference in Chandler on October 31-November 2, 1969. The conference is still in the planning stage and further details will be provided when available.

SECTION ON ECONOMIC ASPECTS OF MEDICARE

Fourth Medicare Fee Survey

Dr. Caldwell reviewed the fourth Medicare fee survey conducted during February. This report is twenty-four pages long and can be obtained at the Central Office.

Letter to Chiefs-of-Staff re: hospital costs

Dr. Caldwell reported that he wrote to the Chiefs-of-Staff of 38 non-profit community hospitals urging them to review their admitting procedures with an eye to reducing the expense of unnecessary tests and examinations. He reported that to date only six responses indicated a real interest in cutting costs, and some were defensive.

SECTION ON MEDICAL REVIEW

In the absence of Dr. Moraca, Chairman, Dr. Reed reported briefly on the problem of paying a group of physicians from Maricopa County General Hospital for nursing home visits of county patients. General discussion ensued on the subject of paying physicians in teaching institutions and the problems associate therewith. No solution, as yet, has been reached.

Utilization of the Medical Review Section by Travelers

It was agreed that when the occasion arises, this section will assist The Travelers Insurance Co. as it does Aetna.

SECTION ON MENTAL HEALTH

Dr. Scott introduced Dr. James D. Van Antwerp, Jr. as the new chairman of this section.

SECTION ON OEO PROGRAMS

Dr. Herbert K. Abrams, Professor, College of Medicine, reported on the planned Neighborhood Health Center in conjunction with the new medical school. Some of his points were as follows:

a. The Center would cover approximately 10,000 people in south Tucson.
b. The county supervisors have given a building for this program.
c. The Center would work in close relationship to the Pima County Hospital.
d. The Center would not duplicate but would work in cooperation with other health agencies.
e. The Center would be a teaching resource to instruct the student within the context of the community and family care.
f. Emphasis would be on the care of the "family."
g. The Center is located in an area with very high rates of diseases, etc., that are preventable. It is essentially a poverty area.
h. The grant comes from the Public Health Service in the amount of $700,000.00 for the first year.
i. Most of the physicians employed will be general practitioners, internists and pediatricians with back-up help in the specialty fields.

SECTION ON REGIONAL MEDICAL PROGRAMS

Dr. Melick not being present, he submitted a written report which was read by Dr. Scott as follows:

"Dr. Richard Flynn forwarded to me a letter from the University of Washington in Seattle, Washington, having to do with medical radio-telephone conferences. His question to me related to the applicability of this type of activity for the State of Arizona and what part the Arizona Regional Medical Program might play in such activity.

"I am sending you a copy of the letter so that you will have it for your file.

"I think this deserves exploration. In view of the fact that I will be in contact with Dr. Donal Sparkman, who heads up the Washington-Alaska Regional Medical Program, and Dr. C. Hilman Castle, who has such an activity going at the University of Utah, I may be able to follow up with more useful information at a later date.

"The two Regional Medical Programs in the United States that are using extensively two-way radio communication for postgraduate medical education are the Intermountain Regional Medical Program in Salt Lake City and the Albany Regional Medical Program in Albany, New York. In both programs, this type of teaching has been going on long enough so it seems a very useful and worthwhile endeavor.

"It would seem to me that in view of the fact that the letter was forwarded to the Arizona Medical Association, it might be worthwhile to return a letter expressing an interest in the activity and asking what can be done to receive additional information and, particularly, what steps would have to be taken in order to implement it in the State of Arizona.

"I think this approach is best, because it would give an initial expression of interest from the Arizona Medical Association, and this, of course, is important in all Regional Medical Programs throughout the country.

"I will follow up on this and give a supplemental report at the next meeting of the Governmental Services Committee.

"In view of the fact that I will be unable to attend the June 5, 1969, meeting of the Governmental Services Committee, I might give you a short report concerning recent developments. A Site Visitation Team from the Division of Regional Medical Programs in Washington arrived in Tucson, and for two days reviewed the progress we have made to date, as well as looking at specific grant applications we now have sent to Washington for definitive action. These grant applications total nine. It is our understanding they will come before the National Council on August 1, 1969. This, of course, depends on funding, which in turn depends on what funds are available. We are optimistic enough at the present time to believe that our program will be adequately funded, but we doubt if the funding will be at the full one hundred percent requested. When the funding does come through, I will report in detail as to what applications were funded and in what parts of the State the activity will begin."

SECTION ON TITLE XIX

Dr. Stannard reported on the meeting of the Joint Legislative Subcommittee to Study Title XIX, held 6/2/69, chaired by Representative Scott Alexander.

Approximately thirty people representing many providers of health care were present including the following physicians: Philip E. Dew, Arthur V. Dudley, Jr., Stanford F. Farnsworth, Richard O. Flynn, Henry D. Smith, and Dale Stannard.

A wide variety of aspects of a Title XIX program in Arizona were discussed.

Representative Alexander indicated that there is no hope for a special session during 1969 due to the Governor's feelings on the subject.

It was determined that Mel Goodwin, Ph.D., Director of the State Comprehensive Health Planning Authority, was to set up a committee to work under the guidance of

Mr. Phil Jones of the Legislative Council in an effort to establish a report setting forth projected costs of a Bare Bones (5 basic services) program, such report to be completed by the end of September so that appropriate legislation can be prepared for introduction in January 1970. His committee would include, but would not be limited to, representatives of Pima and Maricopa County Comprehensive Health Planning groups.

SECTION ON UTILIZATION REVIEW

Dr. Bishop's report on the meetings he was directed to conduct was read as follows:

> "We held a seeries of workshops for Utilization Review at the St. Joseph's Hospital during the month of May.
>
> "Originally, it was suggested that we have a meeting at which time all of those interested in the state would attend, holding it either on a Friday evening or a Sunday afternoon. The Utilization Review Committee of the St. Joseph's Hospital along with the Chief of Staff, balked at such. However, they did extend an invitation that anyone wishing to moderate their meetings was welcome to attend. This invitation was extended to the Hospital Administrators, Record Librarians and anyone connected with any nursing home, rehabilitation center and including all of the osteopathic organizations within the state. The invitation actually was a blank invitation to time, etc. Inasmuch as some organizational work had to go with it, they were invited for either of the Mondays during the month of May.

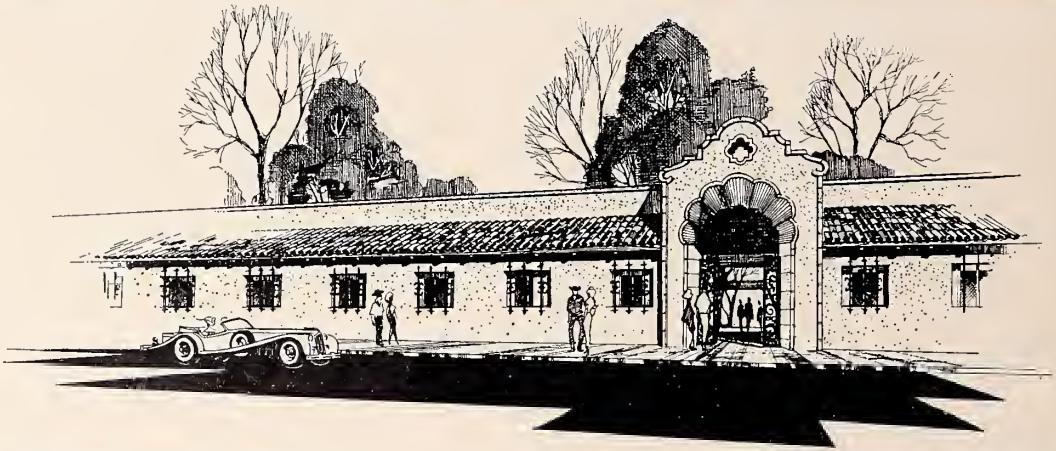
"Due to lack of clerical help and the many things that were timed to take place at the same time, we do not have an accurate roster which was supposed to have been signed there with their title. However, I am enclosing the list of reservations for those four Mondays. As you will notice, the totals were as follows:

May 5, 1969 meeting:	57 reservations
May 12, 1969 meeting:	81 reservations
May 19, 1969 meeting:	45 reservations
May 26, 1969 meeting:	44 reservations

"I would think that, in general, the meetings were quite successful in that many expressed their appreciation for the help that they felt they would get from it.

"May I state in conclusion that the meetings were available for those who wished to attend and that as a member of the Governmental Services Committee, I do not care to and will not participate in further meetings of this type because I feel that what I have done to date should be satisfactory for those who cared to participate or be helped."

Edward Sattenspiel, M.D.
Secretary



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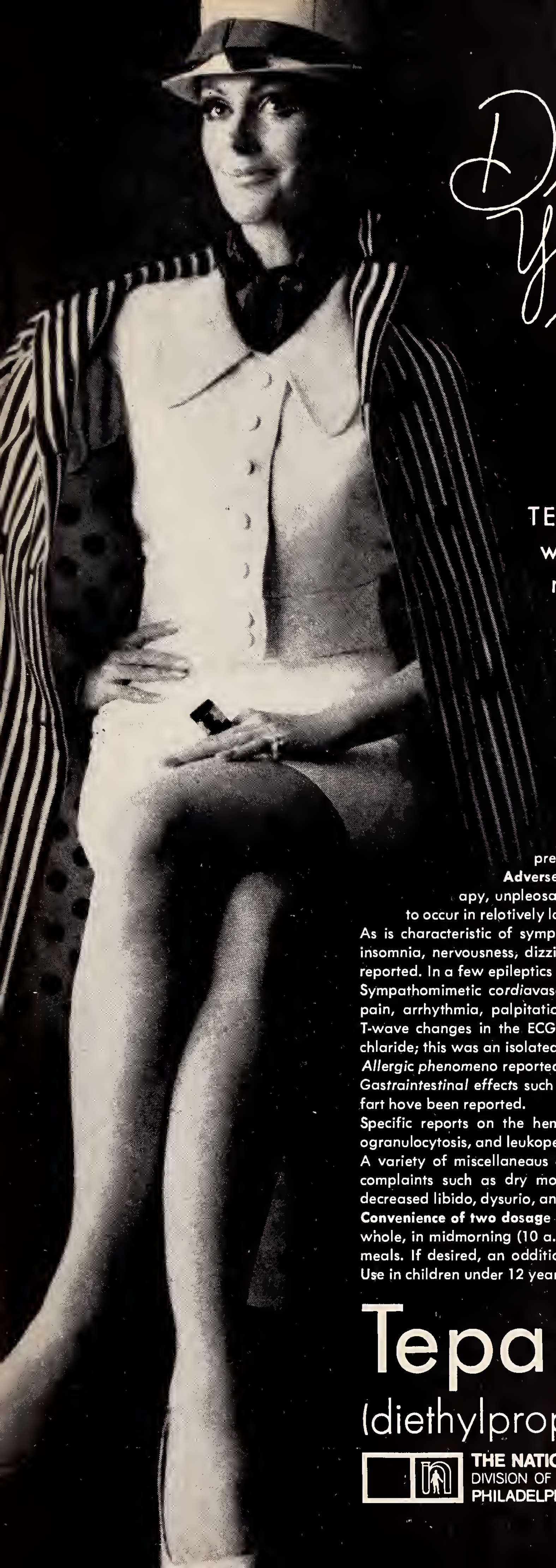

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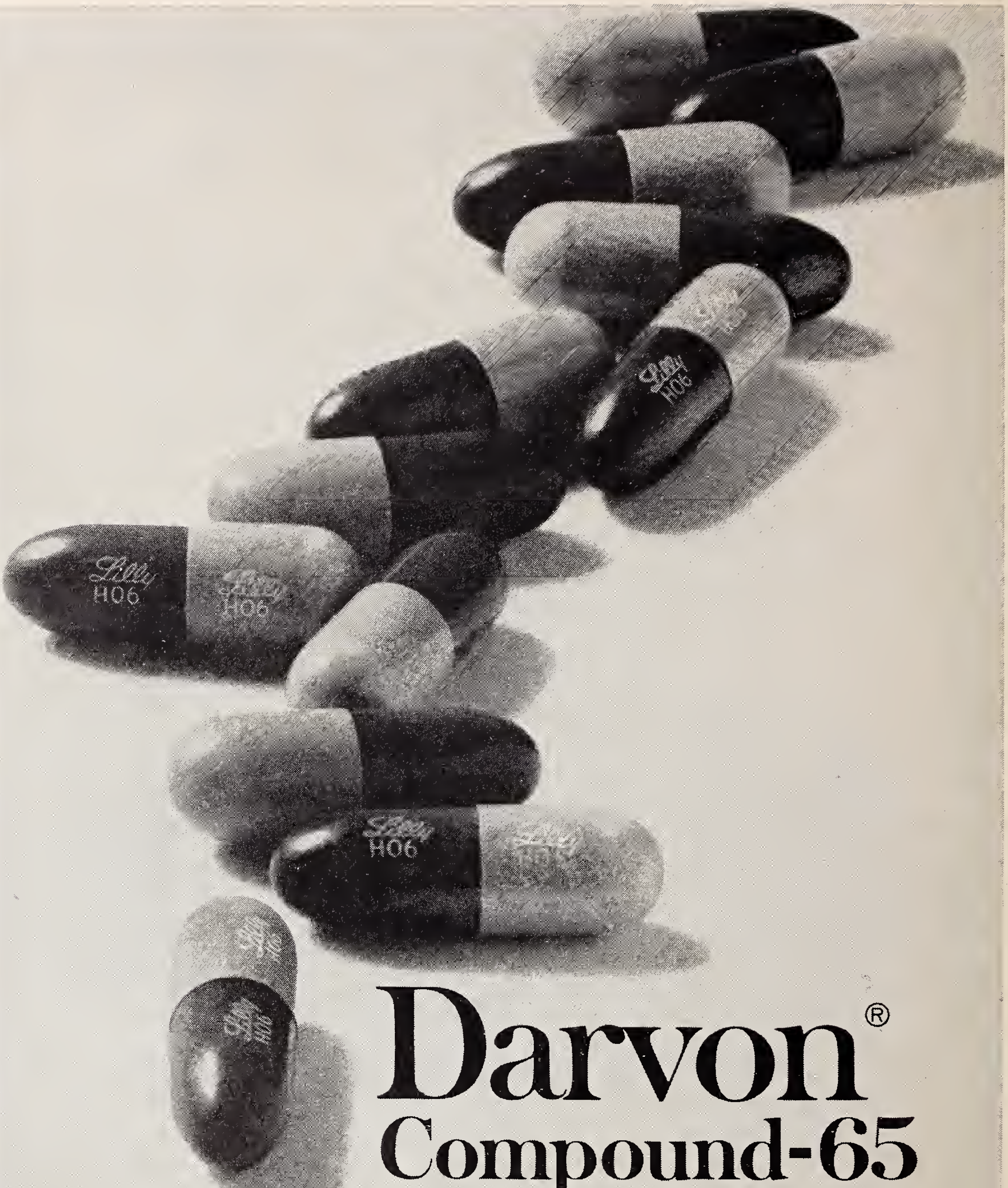

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BREAST TUMORS TREATED BY MASTECTOMY (SUBCUTANEOUS) WITH MAMMARY REPLACEMENT

James J. Berens, M.D., F.A.C.S.*
Lorel A. Stapley, M.D.†

The psychological trauma associated with the loss or disfigurement of a breast is a major concern in breast surgery. This author presents a method in handling breast lesions so that this threat to femininity is minimized.

A long-term need has been recognized for two particular groups of patients with breast lesions. These groups include: (1) patients having multiple or recurrent benign breast tumors; and (2) patients who are felt to have an abnormally high potential for mammary malignancy. Until recently, our weapons included the partial protection of multiple surgical biopsies or the profoundly deforming protection of the traditional simple mastectomy. Until recently, the reluctance of patients to acquiesce to the traditional simple mastectomy has been almost equaled by the lack of courage and fortitude of the physician in recommending such a procedure. A method of managing several types of breast problems is presented which has several advantages: (1) a more complete protection of the patient against invasive carcinoma; (2) a cessation of the anxiety, threat and pain of the recurrent benign breast tumor; and (3) an opportunity to restore the female contour to the patient after tumor therapy is completed.

General Considerations

Subcutaneous mastectomy is a method of treating breast tumors and of preventing future mammary tumors by resection of the glandular portion of the breast. With this technique, an estimated 98 to 99% of the mammary parenchyma and ductal system is removed. A very small amount of mammary tissue remains in the subarolar area for preservation of blood supply to the nipple and conceivably a very slight amount of mammary tissue in the most peripheral portions of the breast could remain in some patients. This operation is not a substitute for the regular or traditional treatment of invasive carcinoma.

The traditional simple mastectomy is performed through a transverse or oblique incision which is elliptical and removes the breast tissue in continuity with the nipple and areola. This operation results not only in loss of the female breast contour but also in the sacrifice of the nipple and areola.

Subcutaneous mastectomy in contrast may be performed through a cosmetically acceptable submammary incision through which the mam-

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*Department of General Surgery
St. Joseph's Hospital, Phoenix, Arizona
†Doctor Stapley died March 2, 1968

mary gland along with its axillary extension may be resected with preservation of all of the overlying mammary skin plus the nipple and areola. With this operation, the patient has the option of restoring a normal female breast contour by using a prosthetic mammary replacement.

Any patient under consideration for subcutaneous mastectomy procedure should be carefully evaluated pre-operatively. The evaluation should include the family history for malignant diseases, the age of the patient, the number of previous breast biopsies by surgical excision or needle aspiration, the histological character of the previously excised breast lesions and the intellectual and emotional response of the patient and her family to the breast tumors. A careful physical examination is of the utmost importance with special attention to the breasts and axillary fossae. Mammography is done as a routine item in the patient evaluation. Any lesion of particular suspicion for malignancy in the breast or axillae is subjected to histologic examination before proceeding with subcutaneous mastectomy.

The patients are instructed in advance that the entire resected mammary gland will be submitted to the pathologist for microscopic examination. They are instructed that an interpretation of invasive carcinoma by the pathologist would be followed by a cancer operation rather than a subcutaneous mastectomy. Our routine treatment for invasive carcinoma is radical mastectomy. Our routine patient's operative consent includes authorization for both simple or radical mastectomy for indeed these operations have resulted in the finding of minute carcinomas that were not detectable on physical examination or mammography.

Indications for Subcutaneous Mastectomy

The following indications have been utilized in selecting candidates for subcutaneous mastectomy. Each patient must be selected on individual considerations, not only by the type of lesion histologically demonstrated, but also by their family history and their personal reaction to the breast lesions. Frequently more than one indication is present in the same patient.

(1) Multiple recurrence of benign breast tumors. This category of patients becomes emotionally exhausted by the repetitive development of breast lesions. The appearance of each new lump in the breast is accepted by these patients as a renewed threat to their very existence until the nature of the lump is clarified. We have had patients who have developed as many as 40 to 50 breast tumors over a period of years that have required surgical excision or needle aspiration with a repetitive fear and anxiety that logically interferes with their normal adjustment to life. This category makes up the largest group of patients who can be helped by simple mastectomy. It is a source of satisfaction to have available a therapeutic approach that can halt the tirade of recurrent breast tumors by subcutaneous mastectomy followed by prosthetic mammary replacement.

(2) Multiple bilateral breast tumors. Some patients have breast tumors so numerous bilaterally that the surgeon is plagued with the decision as to which tumors and how many tumors should be excised in an effort to protect the patient effectively and at the same time avoid a mutilation of her breasts. These patients have frequently undergone previous surgical excisions of breast tumors. Multiple local excisions of so-called dominant lumps gives partial protection against the threat of malignancy but these patients still go home from the hospital knowing that they have lumps which they and their physicians can feel, but which have not been proved benign. A much more effective management is simple mastectomy. Subcutaneous mastectomy with the opportunity for mammary prosthetic replacement offers a more logical treatment and rehabilitation of the patient than the traditional bilateral simple mastectomy.

(3) Breast lesions in patients with strong familial history of breast cancer. The unfortunate women who have had several close relatives develop mammary carcinoma often develop a fatalistic fear of a similar plight and are often faced with an increased statistical likelihood of mammary malignancy. These patients have a legitimate mammary cancer phobia. Patients with a strong familial incidence of breast cancer must of course be individualized in their care. Obviously a young woman with a fibroadenoma of the breast should be treated by local excision whereas a middle aged woman with multiple lesions showing marked hyperplasticity should logically be treated by bilateral mas-

tectomy for both a comprehensive pathological examination of the mammary glands and prophylaxis against the development of invasive carcinoma. This latter group of patients from cancer-ridden families constituted an excellent indication for subcutaneous mastectomy.

(4) Carcinoma in situ of the breast. Lobular carcinoma in situ and intraductal carcinoma in situ are the established examples of this category. The multicentricity and bilaterality of these lesions are becoming better understood. Likewise the progression to invasive carcinoma is being more carefully studied. After examining the transitions between in situ and infiltrating lobular carcinoma, Newman stated, "We are satisfied that when in situ lobular carcinoma is diagnosed treatment should be prompt and vigorous to forestall the ravages of invasive cancer."[1]

(5) Hyperplastic dysplasia of the breast. This category includes the lesions characterized by such marked hyperplastic changes that the pathologist is hard put to delineate between frank malignant degeneration and benign hyperplasticity. This group includes the so-called "gray zone" of breast lesions that are conducive to the pathologist's request for examination of further sections of the tissue and frequently by additional consultations by other pathologists. The responsibility of the pathologist in this group of lesions is profound, for on the one hand the pathologist knows from experience that if he uses the word carcinoma in his diagnosis, the patient will receive a deforming operation and on the other hand if he restricts his descriptive diagnosis to benign terms, the patient will probably receive no more than local excisional treatment and is likely to be dismissed with potentially malignant disease.

(6) Previous unilateral mammary carcinoma. The remaining breast in a patient who has had a previous resection for unilateral mammary carcinoma has a significant statistical incidence of harboring or developing carcinoma. Although a minority of surgeons recommend prophylactic simple mastectomy on the remaining breast, a large number advocate simple mastectomy whenever a benign lesion is found in the remaining breast. The traditional simple mastectomy is a satisfactory operation for these patients already afflicted with a cancer operation on the opposite side. However there are those patients who would prefer to have one breast rather than absence of both breasts. In patients with this attitude, a prophylactic subcutaneous mastectomy with prosthetic mammary replacement may be provided as a prophylactic measure.

(7) Diagnostic mastectomy in the presence of metastatic carcinoma. An example of this category is a lady who two years prior to moving to Arizona had surgical excision of left axillary lymph nodes containing metastatic papillary adenocarcinoma with inability to demonstrate a primary neoplasm in spite of repeat extensive diagnostic studies including excisional breast biopsy on the same side. This patient was somewhat reluctant to have a mastectomy done for diagnostic purposes until presented with the opportunity for prosthetic mammary replacement in the event that no carcinoma would be demonstrable. In this particular patient, although no clinical or mammographic evidence of tumor was present, an area of mild vague increased density was found during the course of the dissection. Biopsy of this area resulted in a diagnosis of mammary carcinoma and the operation was converted to a radical mastectomy.

(8) Miscellaneous breast lesions. Granulomatous mastitis. These lesions result from the rare specific infections or foreign body reactions to injected materials for mammary augmentation.

We have not considered mammary cancerophobia in the absence of any mammary lesion to be an indication for subcutaneous mastectomy. Likewise we have not to this date performed subcutaneous mastectomy for chronic mastodynia of psychogenic origin.

Surgical Technique of Subcutaneous Mastectomy with Mammary Replacement

The objective of the surgeon in performing subcutaneous mastectomy is two fold: (1) the elimination of existing benign tumors; and (2) prophylaxis against future development of breast tumors both benign and malignant. With these goals, it is mandatory to have an interested and capable pathologist perform comprehensive gross and microscopic examination of the resectfig. 1

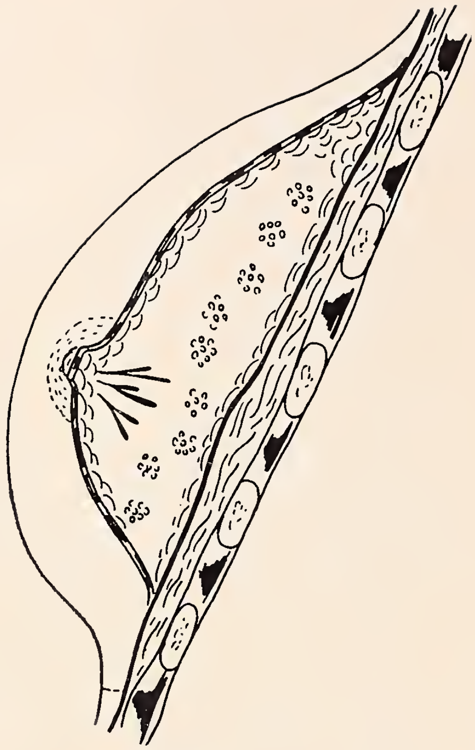

Figure 1
Diagrammatic representation of the breast illustrating essential components of skin, subcutaneous layer and glandular components.

fig. 2

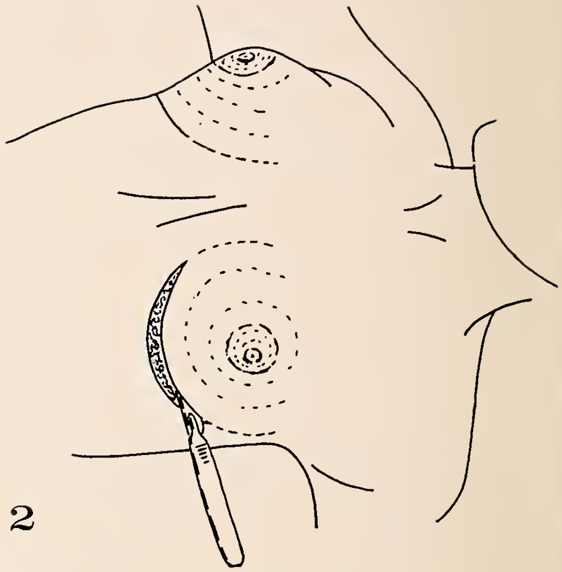

Figure 2
The incision for subcutaneous mastectomy is made parallel to the inframammary ridge.

ed mammary tissue. The excised gland is extensively studied by the pathologist at the time of the operation and frozen section analysis is performed on any local lesions promptly. During the course of the subcutaneous mastectomy dissection, any local areas of suspicion are excised for immediate frozen section interpretation. If invasive malignancy is identified by the pathologist, the planned subcutaneous mastectomy is abandoned and the appropriate cancer operation is performed. Likewise after completion of the operation, the pathologist continues with his comprehensive studies on the resected specimens by permanent section studies.

Subcutaneous mastectomy with prosthetic mammary replacement may be performed as either one or two stage procedures.

The two stage procedure is used routinely by us because of the following advantages. (1) Adequate time is available for comprehensive pathologic studies by the Department of Pathology. (2) The viability of the retained skin, nipple and areola improves and the vascular supply stabilizes. Areas of impaired viability have the opportunity to develop adequate blood supply. (3) The overlying skin shrinks to make a thicker, smoother covering for the prosthesis. The pendulous breast in particular benefits by shrinking down to make a smoother symmetrical covering for the prosthesis. We usually allow one to several months between stages of the operation. The opportune time for the second stage or insertion of the mammary prosthesis is demonstrated by a soft integument with good evidence of viability.

The one stage procedure has the advantage of single hospitalization, operation and anesthetic instead of two, but presents greater risk to the nutritional stability of the skin covering and therefore is more prone to complications.

The first stage of the operation consists of bilateral subcutaneous mastectomy. This is performed through an incision parallel to the inframammary ridge of the breast. (Figure 2) The incision is carried down to the chest wall fascia.

Dissection is then carried in a cephalad direction between the posterior border of the breast and the pectoral fascia (Figure 3) in a medial direction to the sternum, cephalad to the clavicle and lateral into the axillary fossa. Hemostasis is secured with electrocoagulation and fine cat gut ligatures.

Dissection is then resumed at the inframammary incision in a plane between the breast capsule and the subcutaneous tissues. (Figure 4) The mammary gland is thus separated from

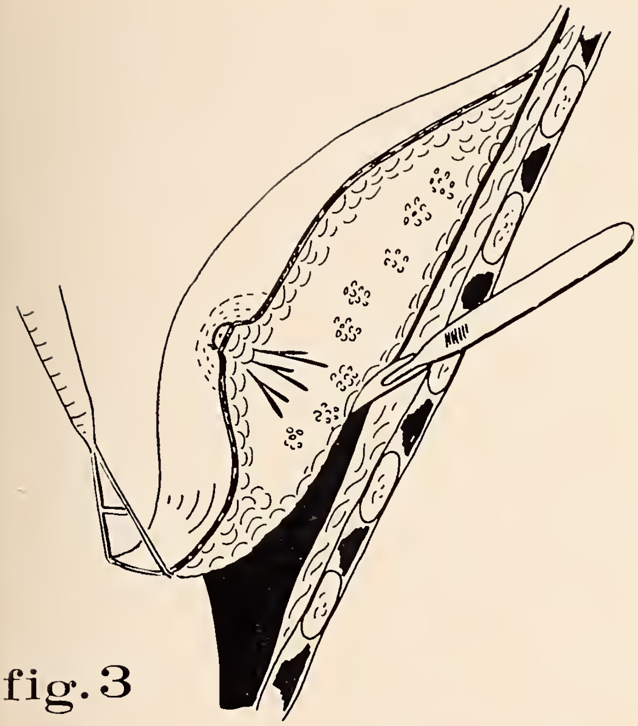

fig.3

Figure 3
Illustration of the deep plane of dissection between the posterior border of the breast and the pectoral fascial layer in subcutaneous mastectomy.

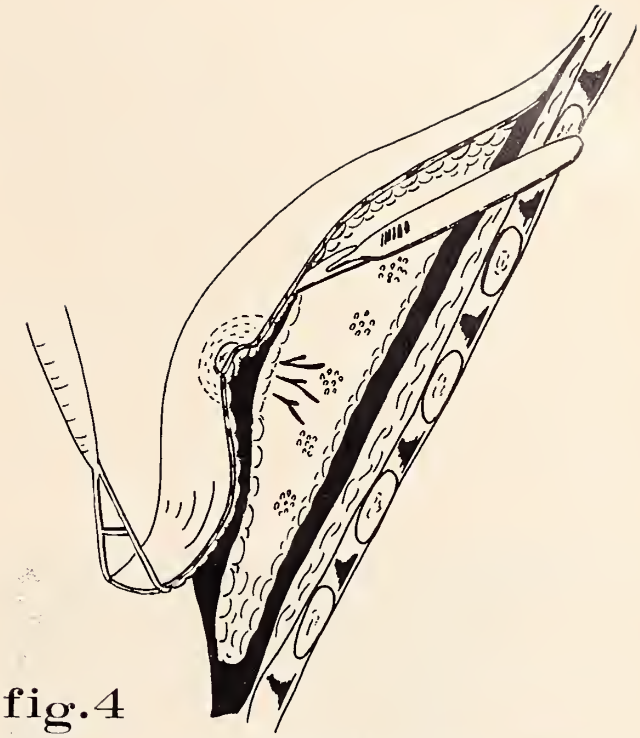

fig.4

Figure 4
Development of the superficial plane of dissection between the subcutaneous layer and the glandular component of the breast in subcutaneous mastectomy.

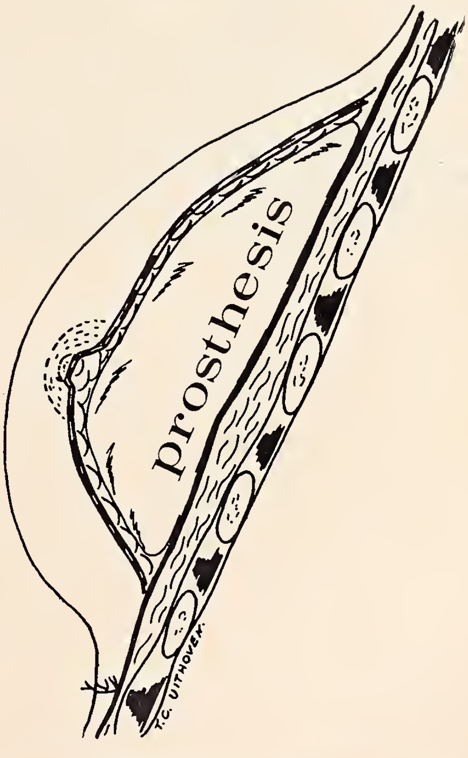

fig.5

Figure 5
Diagrammatic representation of the replacement of the glandular portion of the breast by the mammary prosthesis.

the overlying integument. The dissection is done by both sharp and blunt techniques. Special attention is given to the dissection beneath the nipple and areola, in an effort to preserve the blood supply to this area. The circumareolar plexus of veins is usually quite evident during this part of the dissection. The glandular portion of the breast is resected including the axillary extension.

During the course of the dissection, we excise any areas of particular suspicion for histologic examination by frozen section technique. In other areas where local lesions were identified either clinically or grossly in the course of the dissection, we place long black silk sutures as identifying marks for the pathologist. After careful hemostasis, the wound is irrigated with saline solution and two wound suction catheters are inserted. The incisions are closed with one or two layers of fine suture in the subcutaneous tissues and a continuous nylon fine suture in the skin edges. Small dressings are applied.

The subcutaneous mastectomy procedure completes the definitive portion of the treatment. After confirmation by the pathologist regarding the absence of any invasive carcinoma, and the establishment of good viable skin in the operative area, the patient is then given the opportunity to decide on proceeding with prosthetic mammary replacement.

Most patients elect to have their feminine breast contour restored with prosthetic mammary replacements. One patient, however, was very satisfied after having bilateral subcutaneous mastectomy to know that she did not have any malignant disease of the breast and did not choose to proceed with prosthetic mammary replacement. She was, however, grateful to have preservation of her nipples and areola. After all, people do appreciate having one navel, two eyebrows, one chin and two nipples.

The second stage of the operation consists of prosthetic mammary replacement. In this operation, a prosthesis of appropriate size is inserted beneath the skin to restore the breast contour. (Figure 5) We have been using the SILASTIC mammary prosthesis (Figure 6) with good results.

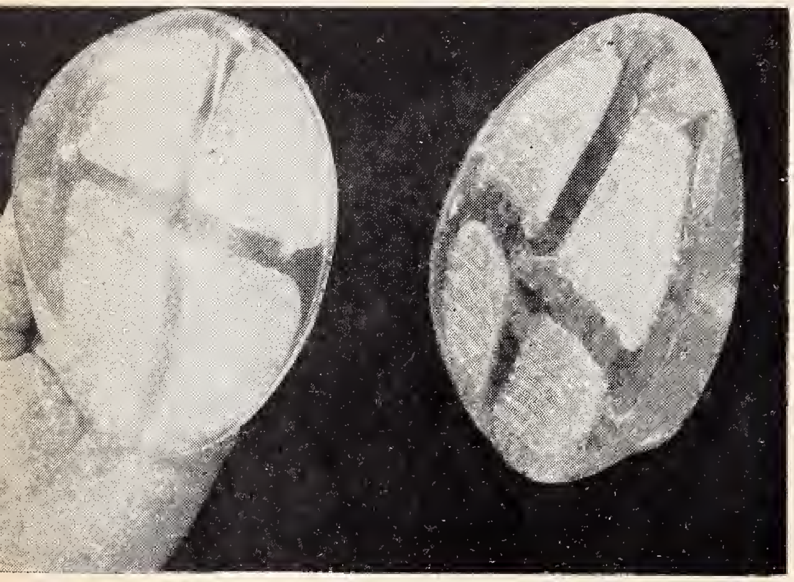

Figure 6
Illustration of the Cronin Silastic type prosthesis utilized in mammary replacement.

The replacement operation is done through the same inframammary incision. The skin and subcutaneous tissues are again mobilized. After careful hemostasis is secured, the appropriate sized mammary prosthesis is inserted. Wound suction catheters are utilized to remove serum. The subcutaneous and cutaneous tissues are sutured as in the first stage procedure. Small dressings are then applied.

Clinical Results

Bilateral simple mastectomy by the subcutaneous route has been performed on thirteen patients. In this small clinical series, ten patients had pathologic changes of benign types, and three patients had significant neoplastic lesions. The data on the latter three patients are summarized.

Patient No. 1. A 43-year-old lady (gravida 3, para 3) complained of diffuse nodularity and mastodynia bilaterally. Breast lesions had been surgically excised at age 17 and 32 years and reported as benign. Examination revealed diffuse vaguely defined nodules in each breast. Mammography was interpreted as consistent with fibrocystic disease with no radiologic evidence of carcinoma. Bilateral subcutaneous mastectomy done February 7, 1967. Examination at the time of operation disclosed a 1.0 cm adenocarcinoma with invasion, multicentric intraductal carcinoma in situ, fibrocystic changes with papillomatosis and intraductal hyperplasia of the left breast. Changes of intraductal carcinoma in situ, fibrocystic disease with papillomatosis and intraductal hyperplasia were present in the right breast. The operation on the left breast was converted to a radical mastectomy. Examination of the axillary lymph nodes was negative for metastatic neoplasm.

Patient No. 2. A 48-year-old lady (gravida 5, para 5) had a grossly cystic tumor excised from the right breast in 1961 with a pathology report of fibrocystic disease with adenosis. In July 1967 a discrete tumor present in each breast was excised and each contained blue dome cysts. The pathologic interpretation was fibrocystic disease with severe intraductal hyperplasia bilaterally.

Although her parents were living in good health and she had a negative history for family cancers, her mother-in-law recently died of breast cancer and her father-in-law recently died of an advanced abdominal cancer. In January 1968 on re-examination, she had no breast symptoms and vague shotty areas of increased density bilaterally but no discrete masses. Mammogram January 29, 1968 showed advanced fibrocystic disease with no evidence of carcinoma. On the basis of the biopsies bilaterally in July 1967 she was offered the opportunity of total mammary gland "biopsy." Bilateral subcutaneous mastectomy was done February 29, 1968. The right breast was found to contain a 7 mm adenocarcinoma with focal stromal invasion and the left breast showed fibrocystic disease with sclerosing adenosis. Two days later the right subcutaneous mastectomy was converted to a radical mastectomy and pathologic studies revealed metastatic adenocarcinoma in two out of 20 axillary lymph nodes.

Patient No. 3. A 45-year-old lady (gravida 1, para 1) had a history in which she estimated that bilateral breast cysts had been aspirated about 40 times over a twenty-five-year period and a benign right breast tumor excised in 1956. Her symptoms were premenstrual pain bilaterally. Examination disclosed multitudinous small tender nodules bilaterally without a dominant tumor. Her family history was negative for cancer. Mammograms done in 1964, 1965 and 1966 were interpreted as bilateral fibrocystic disease with no evidence of carcinoma. Subcutaneous mastectomies were performed January 27, 1967. Pathology studies of the right mammary gland disclosed early lobular carcinoma in situ, fibrocystic disease and sclerosing adenosis. The left mammary gland had marked intraductal hyperplasia, fibrocystic disease and sclerosing adenosis. A month later SILASTIC mammary prostheses were implanted. An uneventful convalescence followed.

Complications

Complications of subcutaneous mastectomy and prosthetic mammmary replacement have been reviewed in a study by Kelly et al.[5] They include hematoma, infection, impaired viability and slough of the skin, wrinkling and displacement of the prosthesis and delayed venous thrombosis.

Discussion

Several types of breast lesions, not involving invasive neoplasm, are best treated by simple mastectomy. In certain breast problems involving recurrent, benign tumors or specific lesions with a high statistical potential for development of invasive neoplasm, simple mastectomy is an effective method of eliminating existing lesions and prophylaxis against future benign and malignant tumors. Increasing experience focuses our attention on the importance of recognizing the multicentricity and bilaterality of many breast lesions. These observations lead to consideration of the benefits of the greater use of bilateral simple mastectomy.

Breast lesions which are treated as effectively by subcutaneous mastectomy as by the traditional simple mastectomy allow particular benefits to accrue for the patient. Although subcutaneous mastectomy is an old operative procedure, newer developments provide an opportunity for these patients to restore a normal female contour by prosthetic mammary replacement. Several plastic materials have been utilized for prosthetic replacements. The basic experience has been provided by the plastic surgeons in their work with mammary augmentation and mastectomy for benign lesions.[2, 3, 4] The prosthesis developed by Thomas D. Cronin, M.D.[3] with the Dow Corning Co., consisting of a soft medical grade silicone (SILASTIC) membrane filled with a jelly-like form of SILASTIC, has been used in our patients.

The experience of performing subcutaneous mastectomies in thirteen patients is encouraging, particularly in identifying significant neoplastic lesions that are not otherwise identifiable clinically. In this small series, two patients were found to have small invasive carcinomas, and one patient to have lobular carcinoma in situ. None of these three patients had neoplastic lesions that were clinically palpable or were identifiable on review of their mammograms. In the two patients with small invasive carcinomas, the simple subcutaneous mastectomies were converted to radical mastectomies.

Our initial experience in a small series of patients stimulates interest in further utilization of subcutaneous mastectomy for select patients with breast tumors.

Abstract

A surgical program is presented to fulfill a need for several types of breast lesions which have been a perplexing problem for patient and surgeon. The surgical management consists of two stages. First, subcutaneous mastectomy in which the glandular portion of the breast is removed, along with the pathologic lesions, while preserving the enveloping skin and nipple. If invasive carcinoma is proved absent, the patient may then elect to proceed with the second stage. The latter consists of prosthetic mammary replacement to restore the normal female contour.

The indications for this procedure are reviewed. The patients benefiting from this treatment lie primarily in two general groups:

1. Patients plagued with multitudinous lesions or multiple recurrences of breast tumors; and
2. Patients with breast tumors who have an abnormally high statistical potential to develop invasive mammary carcinoma.

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NEUROFIBROMATOSIS OF THE SCALP

James E. Reeves, M.D.
San Diego

Early, accurate diagnosis is the touchstone of all good medical care. Children should have this service for obvious reasons.

Rudolph Virchow is supposed to have said Friedrich Daniel von Recklinghausen was his star pupil. In 1882 the pupil described the unusual syndrome which bears his name.

Neurofibromatosis is not commonly seen by many physicians. Only isolated reports of bizarre or advanced cases were found in recent issues of many journals consulted. For example: Woyke, Markiewicz and Tegi[1] recently described two siblings ages 5 and 4 years with extensive neurofibromatosis of the head, trunk, and gums. Their grotesque appearance was frightening.

Only 5 of the 40 cases reported by Conley, Healey and Stout[2] involved the scalp. Congenital fibromatosis may cause early death. Levkoff, Gonzalez and Neher[3] reported the death of a 25 day old male infant due to fibromatosis of the chest and trunk.

Clinical behavior of any neoplasm is usually governed by the *true* cell of origin. Frozen section tissue diagnosis of neurofibromatosis is not recommended. Richardson and Dewar[4] believed central incisional biopsy to avoid mutilation, a high index of suspicion, and careful tissue study essential to good treatment of this disease. Neurofibromatosis may vary greatly in type, extend, prognosis and treatment. The long controversy over Albright's syndrome[5] illustrates some of the problems encountered. Fibrous dysplasia of the face or skull can spread to the bones and produce unusual radiographic findings.[6]

REPORT OF A CASE

A previously healthy 4½ year old boy was examined by me on July 12, 1968. He is the second oldest of 4 children. The mother is Chinese-Hawaiian, the father Caucasian-American. The patient and his siblings appear Oriental.

A complete physical examination revealed nothing abnormal except for several cord-like lesions about 2-3 mm in diameter and about 4-5 cm in length over the parietal boss and occiptal areas of the skull. The lesions moved freely beneath the skin and were not painful to pressure. No pigmentation of the skin was found. Radiographs of the bones of the skull and films of the chest were considered normal for his age and sex. A complete blood count and urinalysis indicated no abnormalities.

On August 26, 1968 under general anesthesia a segment measuring 2 mm by 2 cm was excised. The removed specimen was pale, tortuous, and relatively avascular. Microscopic sections were reported to show delicate, palisaded eosinophilic fibers — probably benign — consistent with neurofibromatosis. Figure 1 represents a typical pattern seen.

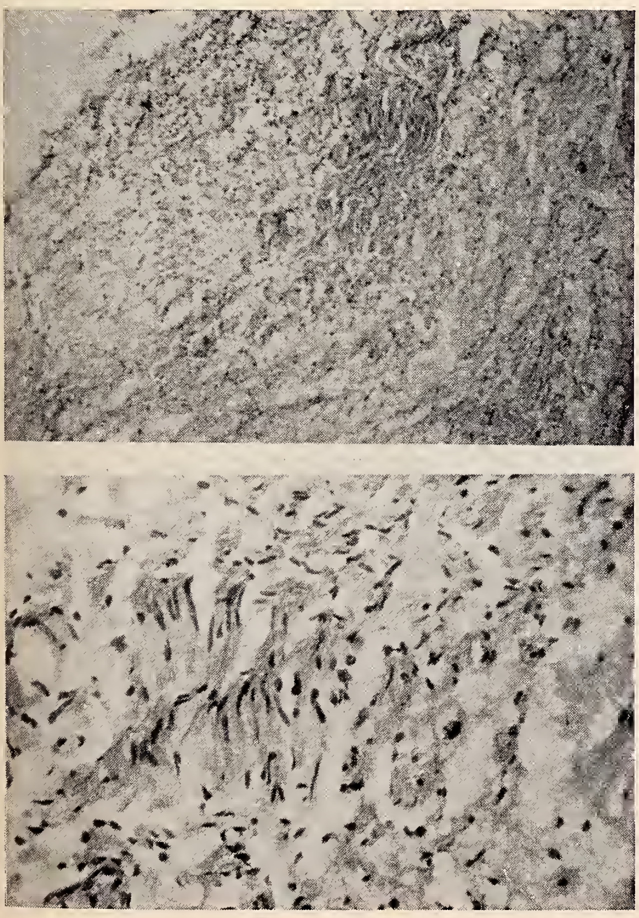

Figure 1

No mast cells were noted on microscopic examination. Baroni[7] believes the number of mast cells is usually greater in neurofibroma lesions than in neurilemmoma. This conclusion was based on a comparative study of 18 nerve sheath tumors. The biopsy wound healed quickly. Except for the remaining original lesions, no change has been noted in this child on follow-up examinations.

I hope this brief case report will stimulate new interest in an old and fascinating disease.

ACKNOWLEDGEMENT

Photomicrographs were made by the Sumerlin Memorial Laboratory, Donald N. Sharp Memorial Hospital, San Diego.

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President's Page

DOG DAYS

Dog Days have arrived. It is too hot to go outside, I don't feel like working, so the only thing left is to sit back and daydream. An interesting pastime is to think up good rejoinders to our critics. These are the things you would like to say to the editor of the newspaper after reading a particularly slanted news article or the brilliant thoughts you have five hours after an argument, after you are home in bed. Medicine has many critics so there is no end of areas where you can work.

Newspaper stories give the biggest challenge. Recent headlines in the morning paper stated doctors were being arrested for abusing Medicare. In reading the article quite carefully, you found that six people in the United States had been arraigned, three of these were "doctors." Of the three, two were from professions other than MD and one who just claimed he was a doctor. There is very little defense for a slanted news article such as this, except hopefully to keep our own fees within the UCR concept.

Congress is upset with doctors because their medical welfare programs are costing three times what their actuaries stated they would cost. (It is interesting that the AMA actuaries in their testimony before Congress were quite accurate in their estimates of total cost.) Since you can't cut administrative salaries or decrease benefits to the voters, doctor fees are about the only things that are left. It is worthwhile sometimes pointing out to these critics that medicine was against this program, even though it couldn't help but increase the income of the doctors.

We are being characterized either as dupes or hand-maidens of the pharmaceutical industry. Dupes because we are getting all our postgraduate medical education from the detail men, and do whatever they tell us to do as far as their products are concerned. Then we turn around and support the drug industry in their fight on trade name or generic equivolency. It is interesting that in the space program you never hear a generic name mentioned. When it comes to drugs to go along with the space capsules, even the Feds realize where quality really counts, that the generics just don't have it.

These are but three examples. All you need do is read the paper or the news magazines, then you could really set the critics straight if you could just get to them. Fortunately, with the start of school in September I won't have time for these fantasies, and Dr. McGrath can quit worrying about me until next August.

Richard O. Flynn, M.D.
President

Dean's Page

PERSONNEL – THE DEPARTMENT OF SURGERY

The first mission of the College of Medicine—to provide outstanding educational opportunities – is inseparable in the surgical sciences from another objective – to provide the best service to patients which is available today. Faculty who have been introduced in this column, as well as those who will be recruited in the months ahead, have been selected as models for the medical students because of their special skills in taking care of sick and injured people. A second qualification – experience in and dedication to the goals of higher education – further enhances their value to the University of Arizona. Nothing could be further from the truth in a modern department of surgery, than the old adage – those who can, do, while those who can't teach. The modern teacher of surgery must be involved deeply in the day to day care of sick human beings if he is to be effective in his relations with students. Thus it seems appropriate to introduce the faculty by reviewing their clinical interests and accomplishments.

Beginning July 1, the Department of Surgery will conduct clinical programs in the Tucson Veterans Hospital and the Davis-Monthan Air Force Base Hospital. Instruction for medical students and residents will be conducted in two major sections. These will be a general surgery section, with a special unit for organ transplantation, and a plastic surgery section, with a special unit for restorative hand surgery. Additional specialties will be added as rapidly as possible.

In addition to the Head, four full-time faculty members have been appointed. They are Dr. Charles F. Zukoski, Dr. William C. Trier, Dr. John W. Madden and Dr. Charles L. Witte. Eight residents arrive July 1 to complete the clinical service.

General surgery and transplantation will be under the direction of Dr. Charles F. Zukoski. Dr. Zukoski is a graduate of Harvard Medical School; he received his surgical training at the Roosevelt Hospital in New York and at the University of Alabama. He spent additional time in the study of transplantation surgery at the Medical College of Virginia and then became a full-time member of the faculty at Vanderbilt University. Dr. Zukoski is an internationally recognized leader in the field of renal transplantation. As Professor of Surgery he will lead a general surgery section and develop a transplantation unit with special emphasis on cadaveric kidney transplants.

Dr. William C. Trier is Associate Professor of Surgery and Chief of the Plastic Surgery Section. Dr. Trier is a graduate of New York Medical College and received his training in plastic surgery at Barnes Hospital in St. Louis. He was Chief of Plastic Surgery at the National Naval Medical Center in Bethesda before joining the full-time faculty of the University of North Carolina. His special interests are head and neck cancer, cleft lip and palate, and cosmetic surgery.

Dr. John Madden is Associate Professor of Surgery and will direct the unique Division of Surgical Biology. Dr. Madden is a graduate of Harvard Medical School and the Massachusetts General Hospital surgical program. He has taught at the University of Pennsylvania and at the University of North Carolina. His special clinical interests are in reconstructive surgery of the hand.

Dr. Charles L. Witte is Assistant Professor of General Surgery. He is a graduate of New York University and received his surgical training in that institution. He has been a member of the medical faculty at Washington University School of Medicine in St. Louis, where his special interests have encompassed the surgery and physiology of the gastrointestinal tract. His most outstanding contributions have been in the study and treatment of hepatic cirrhosis.

The faculty and staff which is being assembled within the Department of Surgery have expressed to many of you their appreciation for the privilege of becoming a part of the tradition of excellence which characterizes Arizona Medicine. In addition to contributing their support to existing programs, wherever it is reasonably possible to do so, they anticipate adding new dimensions of service, education, and research productivity to the efforts already being contributed toward these objectives in the state.

Monte DuVal

STRENGTH OF CHARACTER

William B. McGrath, M.D.

Here is a man of character, a man of moral firmness and principle. He fulfills all of his obligations to the best of his ability and he will not step down from the iron-railed trolley of rectitude. Now why can he not get rid of anxiety?

If he is a perfectionist we might say that his conscience is muscle-bound, inefficient because of tension and impaired elasticity. It is true that the perfectionist can never attain perfection. However painstakingly he tries, he cannot quite avoid some sins of omission. Hence even when he has more than merited his leisure, he still cannot fully relax.

The implication so far is to the effect that the perfectionist should adopt more flexible and tolerant attitudes.

No. He probably couldn't lower his standards in the first place. And if he could, a sense of loss would just increase his uneasiness.

This matter of conscience or superego needs a wider view. We do know the difference between right and wrong. The moralist has put almost exclusive emphasis on aspects of restraint: the avoidance of evil, the fear of transgression. Psychologists have reinforced this emxiety. As a result we practically measure strength of character by the ability to resist temptation.

Surprisingly a man who is most conscientious in this negative sense (do no wrong) may still have a very weak character. It is out of balance.

Conscience should not be just a heavy bucketful of prohibitions. As that half of the scale goes down, the feeling of goodness does not automatically go up. At the other end of the scale, conscience has to be balanced by a bucketful of permissions.

Real strength of character and corresponding equanimity will come to the perfectionist when he deliberately cultivates superego permission, the affirmative aspect of conscience. His instincts and his experience will be quite reliable lanterns.

In this context gladness is the opposite of guilt. One must practise and practise, practise in a thousand instances, letting one's self do the things that he will be glad he did. Within ethical and realistic limits, of course, he must allow himself no procrastination, no excuse, no rationalization for failure to do what he says he wants to do.

A person needs to pay close attention to his own wishes, whatever their degree of consequence. If a man says to himself, "Tonight I want to take a half hour to listen to music," then let him make sure that he will listen to music. If a man thinks, "I'd like to express appreciation or pay a compliment," he must do so. Whenever he lets inconveniences or shyness interfere he is weakening his character.

The anxious perfectionist talks himself out of doing most of the innocent and enjoyable things that occur to him. He will not reach for the things that would make him happy. He cannot accept the hospitality of the world.

Ambition, for a good example, is not driven by will power and grim determination. No; it is released by superego permission. (President Kennedy almost personfied this truism: because he was brought up to feel entitled to the best of everything he did not seem to hesitate to embrace the best of everything).

The conscientious person will do what he is supposed to do. Away from duty he must teach himself then to use the same strength in doing what he wants to do. He will not try to feel good just by avoiding wrong — but also and more so by doing right; i.e., by going ahead and doing whatever makes him glad. No longer grounded by an unbalanced superego, he will feel less anxious and he will be more securely in command of his own destiny.

WILLIAM E. PLATT, M.D.

by
Audrey D. Stevens

The endless determination, energy, imagination, and intelligence of Dr. William E. Platt, late Arizona Territory and early state physician, can well be illustrated by repeating just one event during the courtship of his first wife, Isobel Romney Platt.

It is said that for quite a period of time young Will had admired Isobel from afar but, because of her father's reputation as an extremely strict parent, he had never attempted to court her. One of the methods employed by Mr. Romney, to discourage his daughter's suitors, was to ask the young man to lead the family's prayer service and later to criticize the suitor privately for his inability to lead the prayer. However, Mr. Romney or no Mr. Romney, prayers or no prayers, young Will could stand it no longer so he dressed in his "Sunday-go-to-meetings" and, early one evening, appeared at the front door of the home of Isobel and her family.

For a short period of time, all went smoothly and the nervous young suitor began to relax and enjoy himself. The enjoyment ended all too soon when Mr. Romney, true to his reputation, called for the family prayer service and asked the lovesick victim to lead the prayers. Will complied with the longest prayer ever said in the Romney home: he prayed for everything on heaven and earth; he prayed for every relation — living or dead; he prayed for every friend or would be friend; he prayed for every leader of the Church and ended by praying for most of the federal, state and local goverment officials. After an interval, Mr. Romney became tired of the prayers and tried to stop the service by frequently interspersing an "Amen," but Will prayed on and on and on. Mr. Romney's "Amens" became louder and louder — Will's prayer became longer and longer. The result? Will was never asked to lead the prayers again! Shortly thereafter, with the provision that they would delay their marriage until Will was able to provide for a wife, Mr. Romney consented to their engagement.

A few months after Will's "prayers to end all prayers," the Romneys, Platts and a few other Mormon families moved from St. George, Utah to St. Johns, Arizona, where the hero of this story worked at many jobs. In fact, he worked the greater part of every twenty-four hour day. He worked in the horse and saddle business; he raised a few head of cattle; he set type for the village newspaper; he worked in the Mormon co-op; and in his spare time he worked in the village drug store. This continued for approxi-

mately two years and was climaxed by his serving, as a government messenger on a special mission to Fort Apache. This trip, which earned his One Hundred Dollars, was especially hazardous as the countryside was reputedly infested by hostile Indians. Upon his return he accompanied a few relatives, friends and Isobel back to St. George to celebrate Christmas (1882). They were married a few weeks later.

After returning to St. Johns the Platts lived in the back of the drug store where Will was employed. Later he owned the drug store and was also the St. John's Postmaster. From 1885 and until Dr. W. T. Dalby left St. Johns, Will studied medicine and worked under Dr. Dalby. When Dr. Dalby moved, Will, without a degree, practiced medicine, as quite a few students of medicine did in those early days. Since he was the only citizen in St. Johns that had any knowledge of medicine his medical assistance was deeply appreciated by all.

About 1892, the Platts sold their interest in a herd of sheep and their other possessions, leased the drug store and moved to Kansas City. There Will began his lifelong ambition to obtain a degree in medicine. To help pay expenses, when he was not studying or attending classes, Will worked as a janitor.

His last year of medical school was at the University of Louisville, where he graduated (1894) with honors. The Platts immediately returned to St. Johns and Dr. Platt practiced in St. Johns and the surrounding territory for six years. During that period, he also ran his drug store, learned five Indian tribal languages and re-invested in a one-third interest in a herd of sheep.

About 1900, Dr. Platt, Mrs. Platt and their nine children moved to Safford. Immediately upon their arrival Will opened a drug store which soon became one of three. The latter two were located in Thatcher and Pima.

Telephones were a rarity in Safford as well as in the rest of Arizona Territory. To help overcome this lack of communication, Dr. Platt had a schedule of days that he rode, in his horse and buggy, around the countryside. Any patient who needed him was told to hang a tea towel on their gate as a signal that the doctor was needed. At times, several families would be waiting at the same house to see him. When necessary, he would spend the night with his patient serving as doctor, nurse and sometimes as the cook.

On one occasion, he had to use a patient's butcher knife and other kitchen utensils to perform an emergency appendectomy. (The patient lived to attend Dr. Platt's funeral.) On another occasion, he found a dying man alone, and beyond medical help. After staying with the patient until he died, the Doctor brought the patient's body back to Safford for burial.

In the forty-two years that he practiced in Safford, Dr. Platt delivered so many babies in both Thatcher and Safford that no one can give the exact number he delivered. Nor can a figure be given for the number of tonsillectomies he performed. For example in 1918, shortly after the death of Isobel Platt, with the aid of his three eldest daughters and Dr. T. H. Slaughter of Miami, he scheduled two full days of tonsillectomies. The surgery began at 6:00 a.m. and continued until late at night with the same schedule the second day. It is said that by the end of the second day more than 200 school children were minus their tonsils.

The operating table for the "tonsillectomy clinic" was the Platt's dining room table. However, this was not the first time the table was used for surgery. Nor was the dining room the only room in the house that Dr. Platt used in his practice of medicine. As a matter of fact most of the Platt home was used at some time or other for Dr. Platt's professional practice or for his other business interests. Mrs. Clara Platt Goodman, now of Phoenix, daughter of Dr. Platt, wrote that her brothers and sisters were never certain, from one night to the next, whether they would have the pleasure of sleeping in their own bed or have to sleep with another member of their family. The reason for this was that Dr. Platt also owned half interest in the one and only mortuary in Safford. In addition to this, Safford had no hospital, therefore, the beds at the Platt home might and often were occupied by his patients or by a corpse. (The latter occupant was especially true during the flu epidemic.)

One can judge from this article that Dr. Platt lived, to say the least, a very full life. In his later years, much to Dr. Platt's embarrassment, several testimonial dinners were given in his honor. It is said, however, that his embarrassment was exceeded by his love of parties and social gatherings. At these dinners much was said about Dr. Platt's lack of keeping records of his debtors. Dr. Platt's reply was that he felt that his medical ability was a way of his serving mankind and he therefore depended on his other businesses for financial gain.

Besides the testimonial dinners the Arizona Daily Star of 1939 and 1941 carried articles regarding Dr. Platt. The articles told of the respect and love Dr. Platt so well deserved and had from his fellow Saffordites.

His life also served as an example of such a wonderful way of life that two of his daughters became registered pharmacists and three of his grandsons became doctors.

In 1941 Dr. Platt died at the age of 82. Besides the patients who dearly loved him, he left as survivors: his second wife, Blanche Cleora Murdy; nine children; several grandchildren and enough stories regarding his career and his family to fill a good sized book.

ACKNOWLEDGMENT

A hearty thank you to the residents of Safford who asked me to write this article and helped supply material for same. Special appreciation to Mr. Don Pace and Mrs. Clara Platt Goodman, daughter of Dr. William Platt.

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Topics Of Current Medical Interest

OUR NEW BUILDING AS IT LOOKED ON JUNE 27, 1969

DO YOU KNOW THIS MAN ??

Information urgently needed concerning the whereabouts of Wesley Harold Zahl, M.D., missing since April while traveling from California to Wisconsin. A long-time resident of South Milwaukee, Wisconsin, Dr. Zahl had lived in Burbank, California, for the last six months. He is 67 years old, 5'10", 160 lbs., hazel eyes (wears eyeglasses) a hemiplegiac without facial paralysis but with right arm in rigid flexed position and slight speech disturbance, walking with aid of a cane. Contact Cudahy Detective Bureau, Cudahy, Wisconsin.

In Memoriam

BERNARD M. LIPSCHULTZ, M.D.
1912-1969

On May 29, 1969, Dr. Bernard M. Lipschultz expired at the age of fifty-six years at the Veterans Administration Hospital, Phoenix, where he was the Chief of Medicine.

Doctor Lipschultz was survived by his wife, Inez, two sons, Allen, a resident in internal medicine at the University of Colorado Medical Center, Denver, and Arthur, a medical student at the University of Southern California.

Doctor Lipschultz was born in New York City, received his M.D. degree at the University of Illinois College of Medicine in 1937, and served as a major in the Medical Corps in World War II and later as a colonel in the Active Reserve. Prior to his arrival in Phoenix in 1950, he was Chief of Cardiology at the Veterans Administration Hospital in Dallas and Professor of Medicine at the University of Texas Southwestern Medical School. He was a Diplomate of the American Board of Internal Medicine and a Fellow in both the American College of Physicians and American College of Cardiology as well as a member of the American Medical Association, Maricopa County Medical Society, and Maricopa and Arizona Heart Associations. He was a founder of the Cardiac Laboratory at the Good Samaritan Hospital, Phoenix, and of the Integrated Medical Residency Program of the Veterans Administration, Good Samaritan and USPHS Hospitals.

On May 1, 1969, he received a Commendation Award for Outstanding Service from the Regional Medical Director for Veterans Administration Hospitals in Washington, D.C., the only such honor ever awarded to a Phoenix physician.

All of these facts are well known to Bernie's many friends and colleagues and he gained and held their respect throughout his lifetime. I believe, however, that he will be remembered as much by all who knew him for a more special gift and personality. Bernie was a quiet gentle and humble man who unobtrusively "went about his way" with unassuming dedication and competence. In almost twenty years he was the only man whom literally I have never seen or known to become angry despite his significant responsibilities. After learning of his diagnosis and shortened life expectancy, he met those final days with the same uncomplaining courage and dignity he had always exhibited.

In our times, particularly in a world torn by strife, angers, and the need for personal aggrandizement, this man's qualities took on an extra dimension of grace and humanity. All who have known him will indeed miss him!

Lee Ehrlich, M.D.

Letters to Editor

June 3, 1969

Patrick P. Moraca, M.D., Chairman
Medicare Medical Review Committee

Dear Doctor Moraca:

Reports from Jim Blazek of our Phoenix office and Dr. Hardie on the May 26 meeting with Dr. Harris and his group are most encouraging. Jim also sent me a copy of your May 28 letter to Dr. Harris outlining the Medical Review Committee's recommendations.

I would like to take this opportunity to belatedly thank you and the members of your committee for the help given us in the administration of the Medicare program in Arizona. As you know, we also administer Part B in several other states; however, the cooperation we have received from the Medical Review Committee in Arizona, and the spirit in which it has been given, has not been surpassed by any group in any other area in which we operate.

We hope that the physicians of Arizona feel, as do we, that working out problems together best serves their interests as well as those of beneficiaries and the overall program.

Sincerely,
R. E. Stewart
Assistant Secretary
Medicare Administration
Aetna Life & Casualty

6TH NATIONAL CANCER CONFERENCE – NOTES

September 1968, Denver

Pre and Postoperative radiation treatment for cancer — refers one to an excellent review in S.G. & O. April-May 1968. If preoperative radiation is given, include all tissue to be operated upon with the greatest dose to the central portion; radiation should include any area where secondary surgery will be necessary; and when surgery is done do not compromise your surgical procedure but be radical. If postoperative irradiation is necessary in general "preoperative irradiation should have been given". All told, only 5 to 10% of the patients will be benefited by the addition of radiation therapy; that is, the group without disseminated disease and those that would not have been cured by surgery alone.

William M. Powers, M.D., Director
Division of Radiation Therapy
Washington University School of
Medicine, St. Louis, Missouri

Tumor specific antigens have been found in animals. The immunization of animals with various tumors may result in delayed growth or even cause the tumor to regress. If the immunizing dose is excessive, the animals die. It is not likely that immunization therapy will prove adequate to eliminate large established tumors but this form of treatment may prove and adjunct in therapy.

Herbert J. Rapp, D.Sc., Chief Biology
Branch, National Cancer Institute,
Bethesda, Maryland

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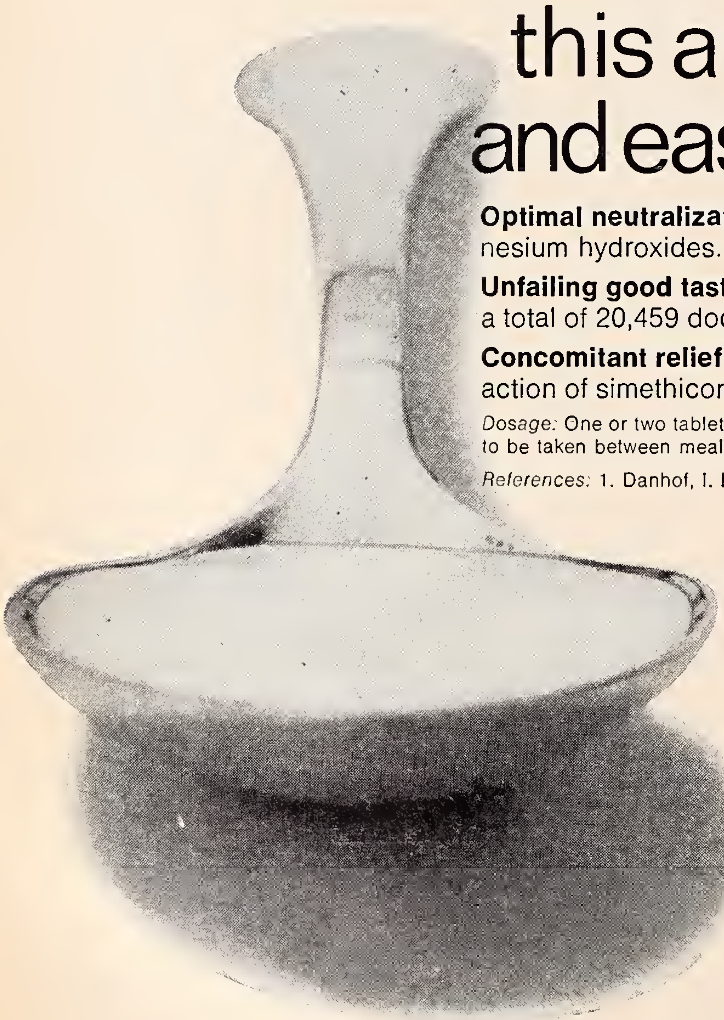

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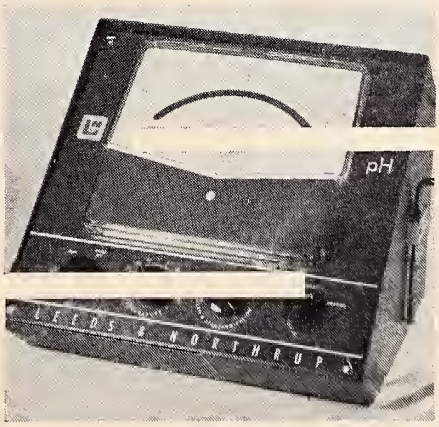

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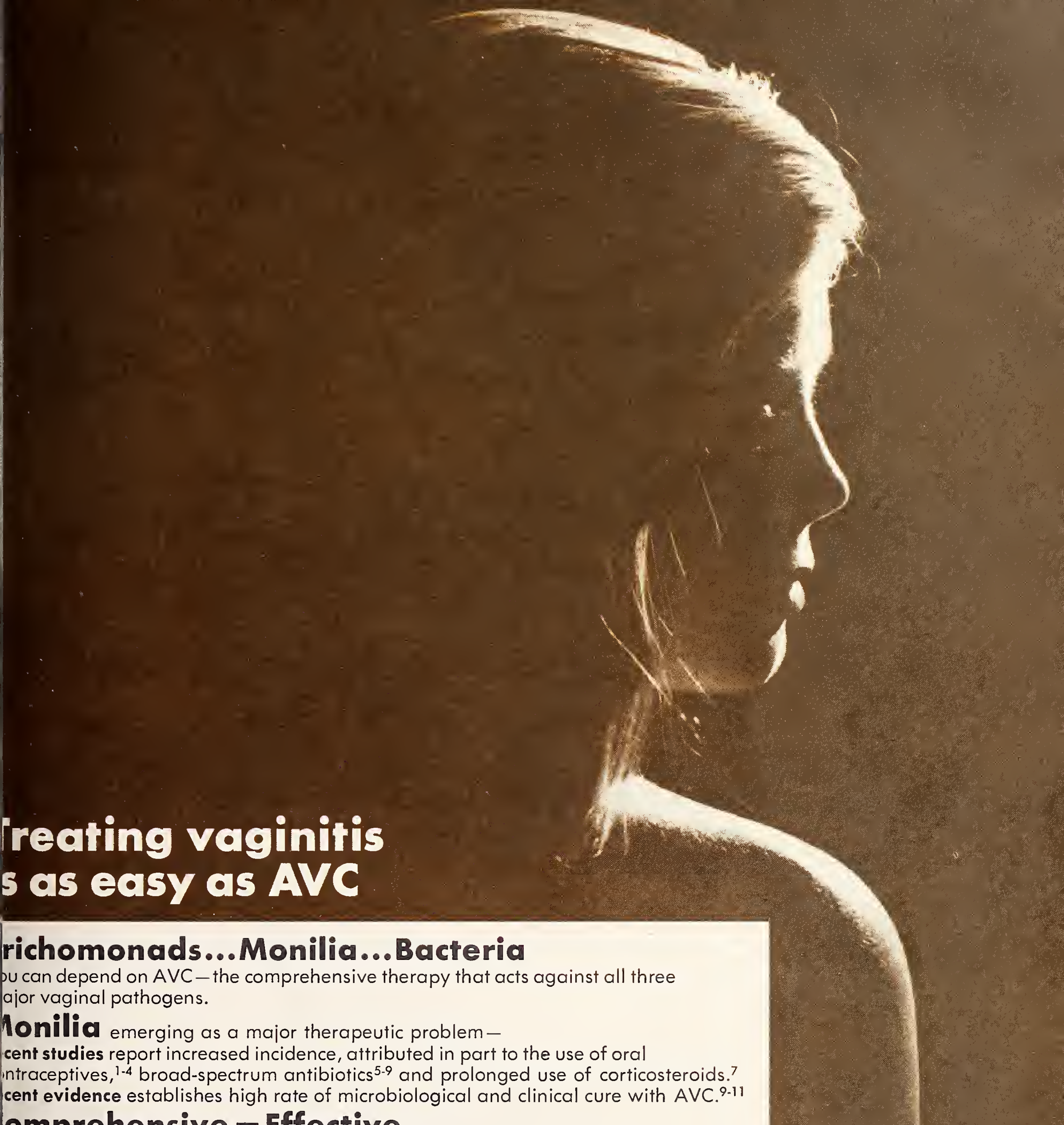

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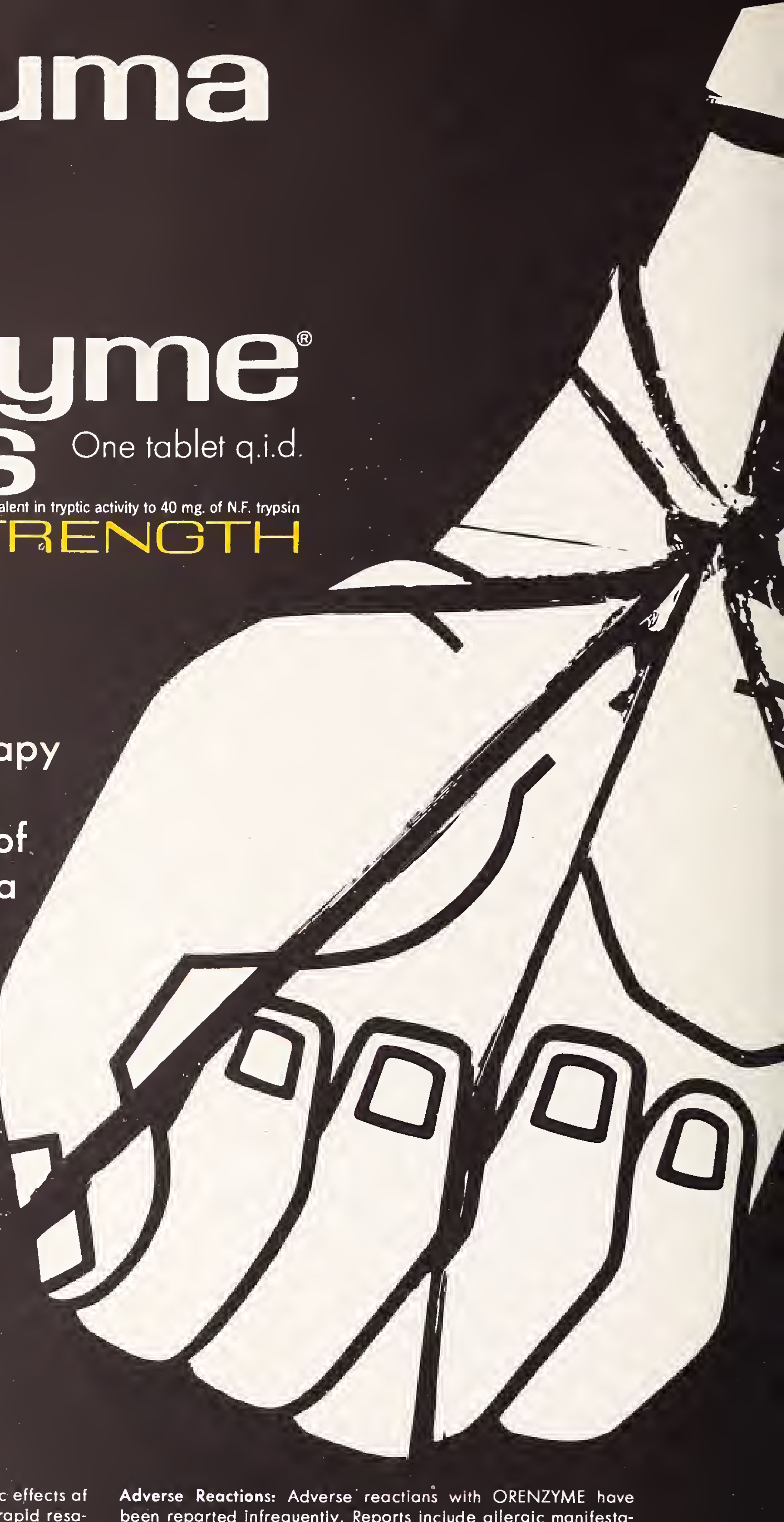

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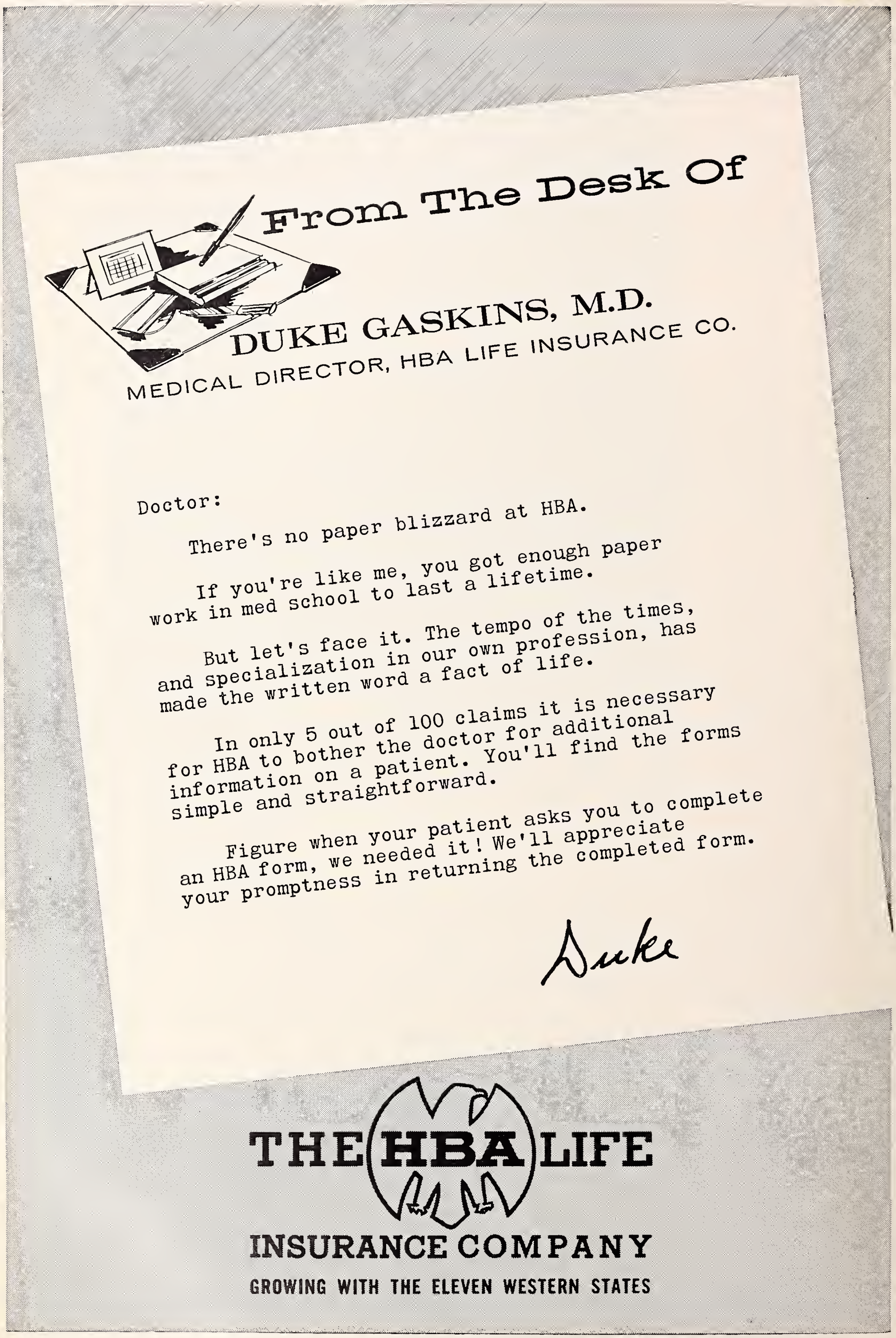

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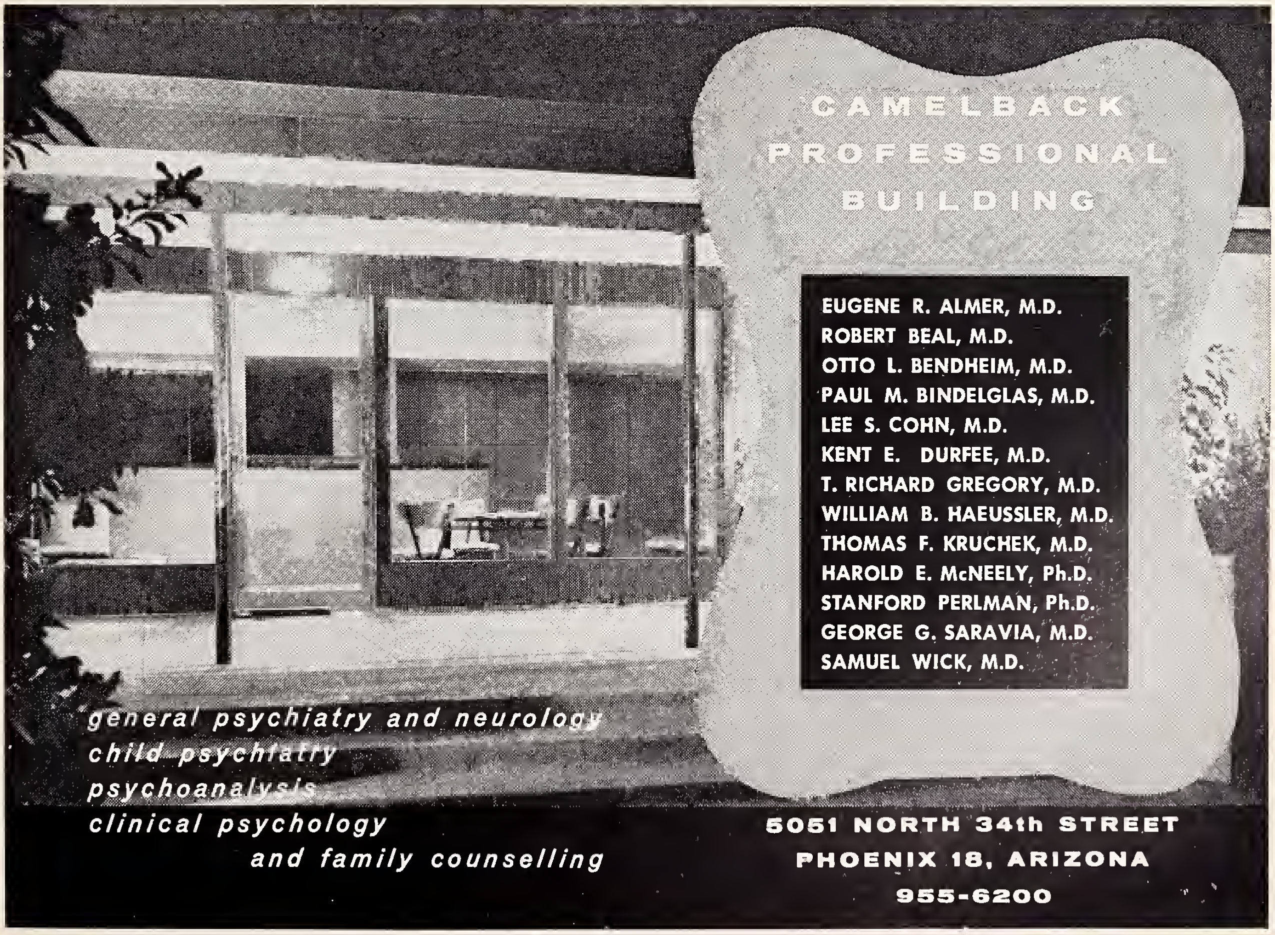

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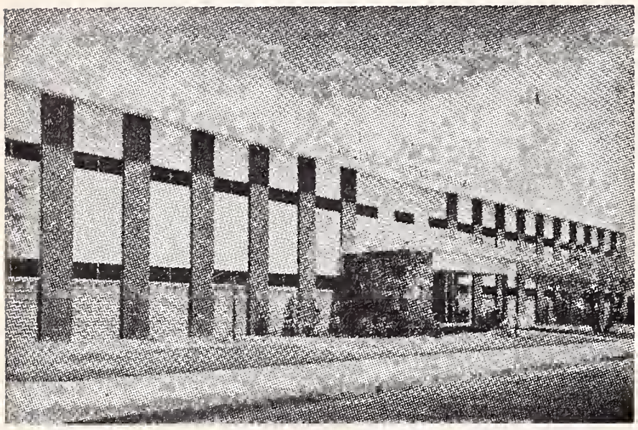

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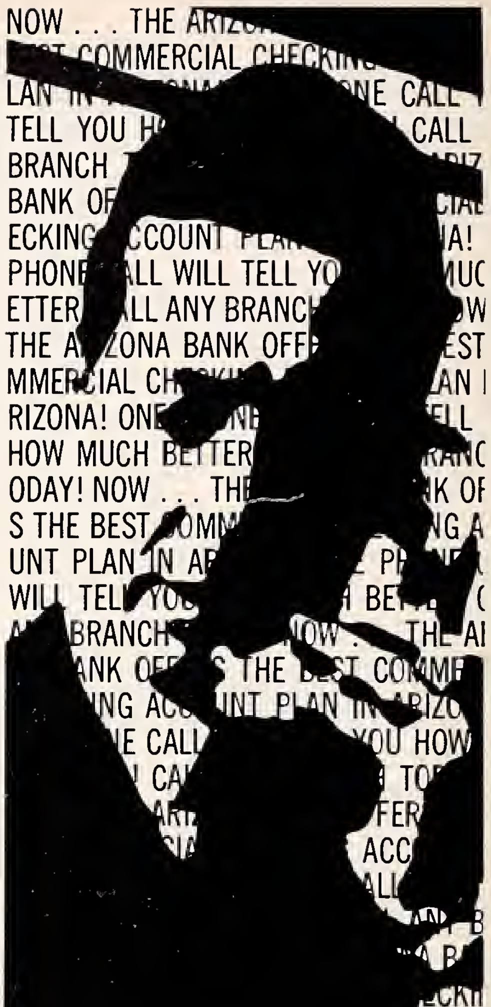

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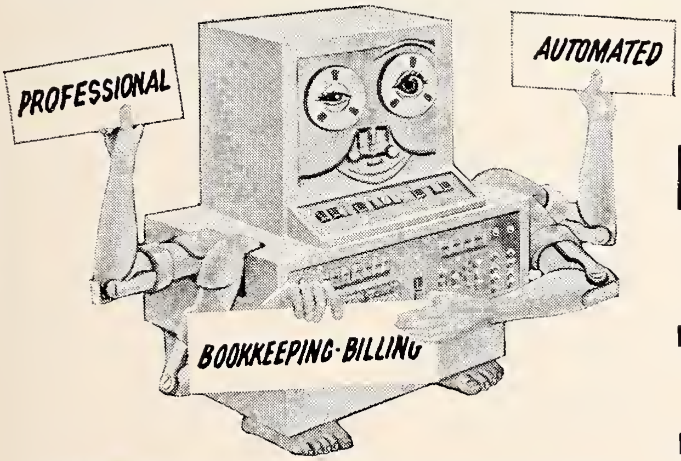

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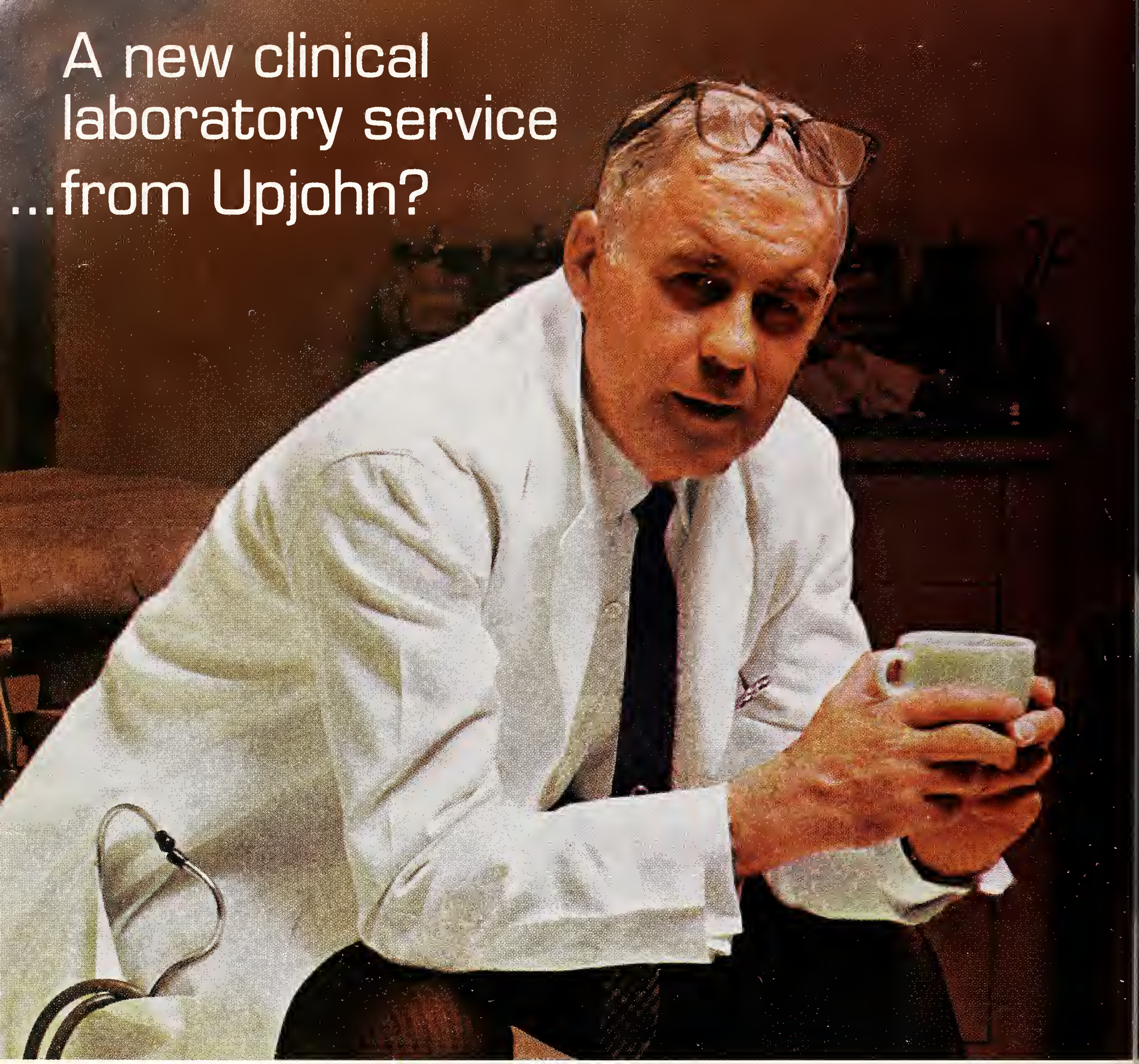

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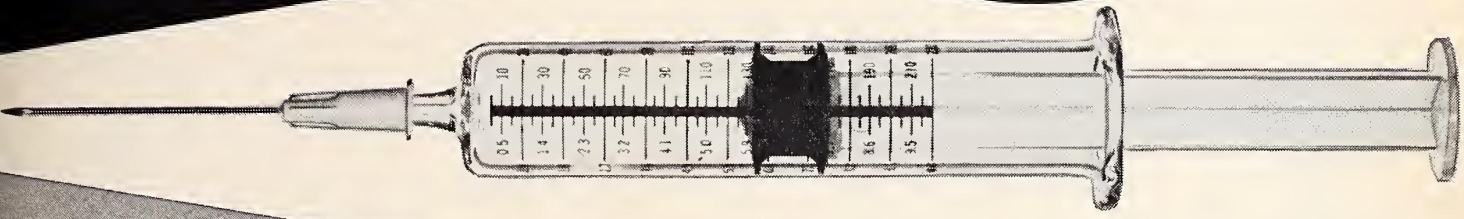

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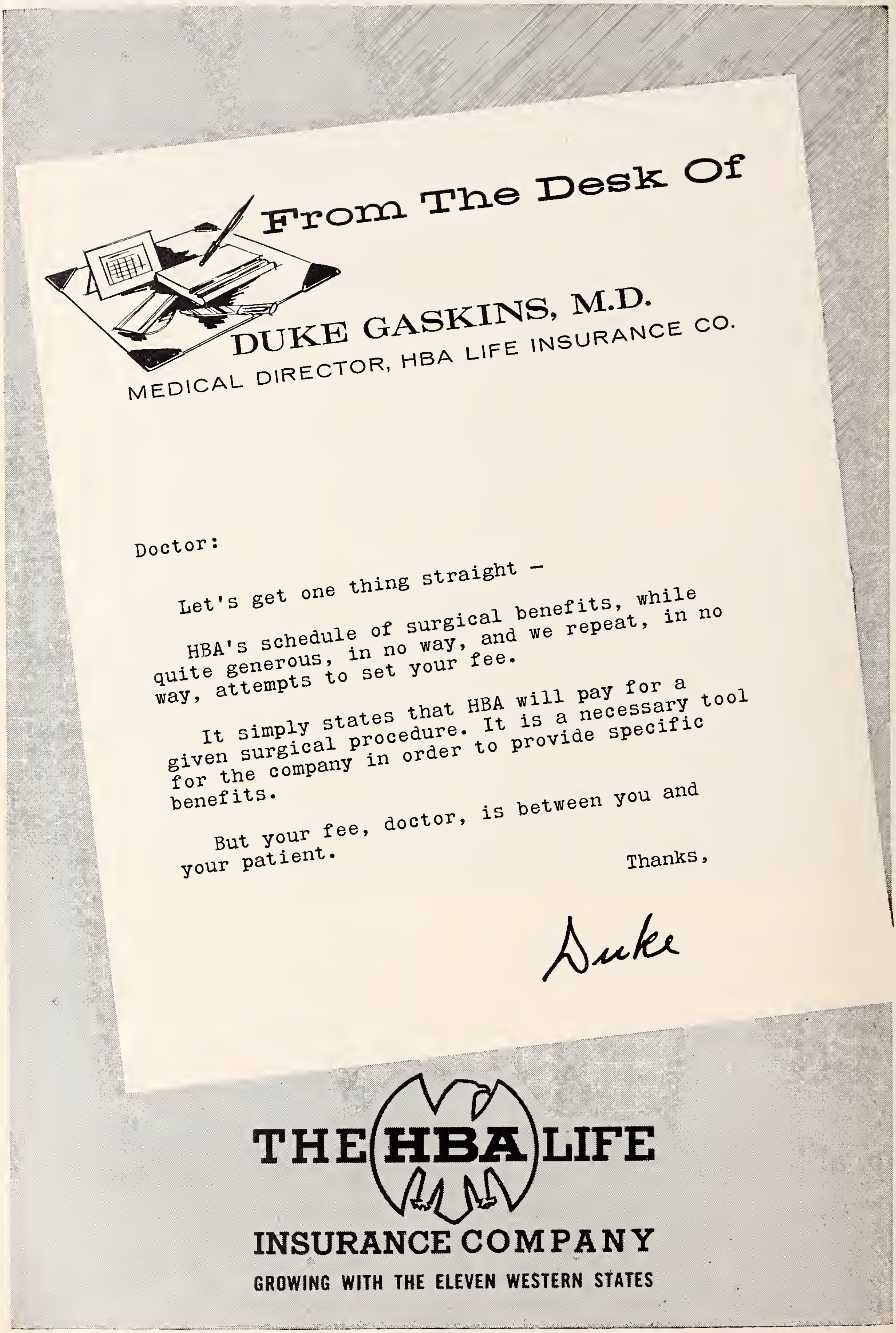

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Published monthly by The Arizona Medical Association, Inc., with offices at 4601 N. Scottsdale Rd., Suite 201, Scottsdale, Arizona 85251. Subscription $5 a year, single copy 50 cents. Second class postage paid at Scottsdale, Arizona, and at additional mailing offices.

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when it's late in life and anxiety and depression coexist...

initial therapy

Triavil® 4-10

Each tablet contains 4 mg. of perphenazine and 10 mg. of amitriptyline hydrochloride

maintenance therapy

Triavil® 2-10

Each tablet contains 2 mg. of perphenazine and 10 mg. of amitriptyline hydrochloride.

appropriate therapy in an appropriate dosage

During the years of declining strength and increasing infirmity, many patients are more sensitive to both the desired response and the unwanted effects of some drugs. That's when low-dosage therapy is needed. And that's when Triavil 4-10, as initial therapy, and Triavil 2-10, for maintenance, can prove particularly useful.

Starting with Triavil 4-10 should help minimize possible dose-related side effects in the geriatric patient with coexisting anxiety and depression. And, subsequently, Triavil 2-10 can increase flexibility in adjusting maintenance dosage.

Activities made hazardous by diminished alertness should be avoided. You will want to inform your patients that the effects of alcohol may be potentiated. Because of the potentiation of other drug effects possible with MAO inhibitors, such agents should not be given concomitantly with Triavil. However, therapy with Triavil can be initiated cautiously two weeks or more after withdrawal of the MAOI drugs. And, until significant remission is observed, close supervision of any seriously depressed patient is, of course, essential to guard against possible suicide. The drug is contraindicated in glaucoma, in patients expected to experience problems of urinary retention, in drug-induced CNS depression, and in bone marrow depression.

Triavil 4-10 & 2-10—tranquilizer-antidepressant therapy especially appropriate for the elderly patient so often intolerant to medication in high dosages.

TRIAVIL® **for moderate to severe anxiety with coexisting depression**

containing perphenazine and amitriptyline HCl
TRANQUILIZER-ANTIDEPRESSANT

For additional prescribing information, please see following page.

TRIAVIL®

TRANQUILIZER-ANTIDEPRESSANT

TRIAVIL 4-10: Each tablet contains 4 mg. of perphenazine and 10 mg. of amitriptyline hydrochloride.
TRIAVIL 2-25: Each tablet contains 2 mg. of perphenazine and 25 mg. of amitriptyline hydrochloride.
TRIAVIL 4-25: Each tablet contains 4 mg. of perphenazine and 25 mg. of amitriptyline hydrochloride.
TRIAVIL 2-10: For use in adjusting maintenance dosage. Each tablet contains 2 mg. of perphenazine and 10 mg. of amitriptyline hydrochloride.

for moderate to severe anxiety with coexisting depression

INDICATIONS: Patients with moderate to severe anxiety and/or agitation and depressed mood; patients with depression in whom anxiety and/or agitation are severe; patients with depression and anxiety in association with chronic physical disease; schizophrenics with associated depressive symptoms.

CONTRAINDICATIONS: Central nervous system depression from drugs (barbiturates, alcohol, narcotics, analgesics, antihistamines); bone marrow depression; urinary retention; pregnancy; glaucoma. Do not give in combination with MAOI drugs because of possible potentiation that may even cause death. Allow at least 2 weeks between therapies. In such patients therapy with TRIAVIL should be initiated cautiously, with gradual increase in the dosage required to obtain a satisfactory reponse.

WARNINGS: Patients should be warned against driving a car or operating machinery or apparatus requiring alert attention, and that response to alcohol may be potentiated.

PRECAUTIONS: Suicide is always a possibility in mental depression and may remain until significant remission occurs. Supervise patients closely in case they may require hospitalization or concomitant electroshock therapy. Untoward reactions have been reported after the combined use of antidepressant agents having various modes of activity. Accordingly, consider possibility of potentiation in combined use of antidepressants. Not recommended for use in children. Mania or hypomania may be precipitated in manic-depressives (perphenazine in TRIAVIL seems to reduce likelihood of this effect). If hypotension develops, epinephrine should not be employed, as its action is blocked and partially reversed by perphenazine. Caution patients about errors of judgment due to change in mood.

SIDE EFFECTS: Similar to those reported with either constituent alone. **Perphenazine:** Should not be used indiscriminately. Use caution in patients with history of convulsive disorders or severe reactions to other phenothiazines. Likelihood of untoward actions greater with high doses. Closely supervise with any dosage. Side effects may be any of those reported with phenothiazine drugs: blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia); liver damage (jaundice, biliary stasis); extrapyramidal symptoms (opisthotonos, oculogyric crisis, hyperreflexia, dystonia, akathisia, dyskinesia, parkinsonism) usually controlled by the concomitant use of effective antiparkinsonian drugs and/or by reduction in dosage, but sometimes persist after discontinuation of the phenothiazine; severe, acute hypotension (of particular concern in patients with mitral insufficiency or pheochromocytoma); skin disorders (photosensitivity, itching, erythema, urticaria, eczema, up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions); peripheral edema; reversed epinephrine effect; endocrine disturbances (lactation, galactorrhea, disturbances of menstrual cycle); grand mal convulsions; cerebral edema; altered cerebrospinal fluid proteins; polyphagia; paradoxical excitement; photophobia; skin pigmentation; failure of ejaculation; EKG abnormalities (quinidine-like effect); reactivation of psychotic processes; catatonic-like states; autonomic reactions such as dryness of the mouth, headache, nausea, vomiting, constipation, obstipation, urinary frequency, blurred vision, nasal congestion, and a change in the pulse rate; hypnotic effects; pigmentary retinopathy; corneal and lenticular pigmentation; occasional lassitude; muscle weakness; mild insomnia; significant unexplained rise in body temperature may suggest intolerance to perphenazine, in which case discontinue. Antiemetic effect may obscure signs of toxicity due to overdosage of other drugs or make diagnosis of other disorders such as brain tumors or intestinal obstruction difficult. May potentiate central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol), atropine, heat, and phosphorous insecticides. **Amitriptyline:** Careful observation of all patients recommended. Side effects include drowsiness (may occur within the first few days of therapy); dizziness; nausea; excitement; hypotension; fainting; fine tremor; jitteriness; weakness; headache; heartburn; anorexia; increased perspiration; incoordination; allergic-type reactions manifested by skin rash, swelling of face and tongue, itching; numbness and tingling of limbs, including peripheral neuropathy; activation of latent schizophrenia (however, the perphenazine content may prevent this reaction in some cases); epileptiform seizures in chronic schizophrenics; temporary confusion, disturbed concentration, or transient visual hallucinations on high doses; evidence of anticholinergic activity, such as tachycardia, dryness of mouth, blurring of vision, urinary retention, constipation, paralytic ileus; agranulocytosis; jaundice. The antidepressant activity may be evident within 3 or 4 days or may take as long as 30 days to develop adequately, and lack of response sometimes occurs. Response to medication will vary according to severity as well as type of depression present. Elderly patients and adolescents can often be managed on lower dosage levels.

Before prescribing or administering, read product circular with package or available on request.

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Editor's Page

TWO MILLION ENGLISHMEN MAY BE RIGHT

In 1948 the National Health Service Act began providing health care for those persons living in England and Wales. When added to the Education Act and the National Insurance Act, this law completed the welfare state structure of Great Britain. The medical service program in England was intended to guarantee health to all as a matter of right.

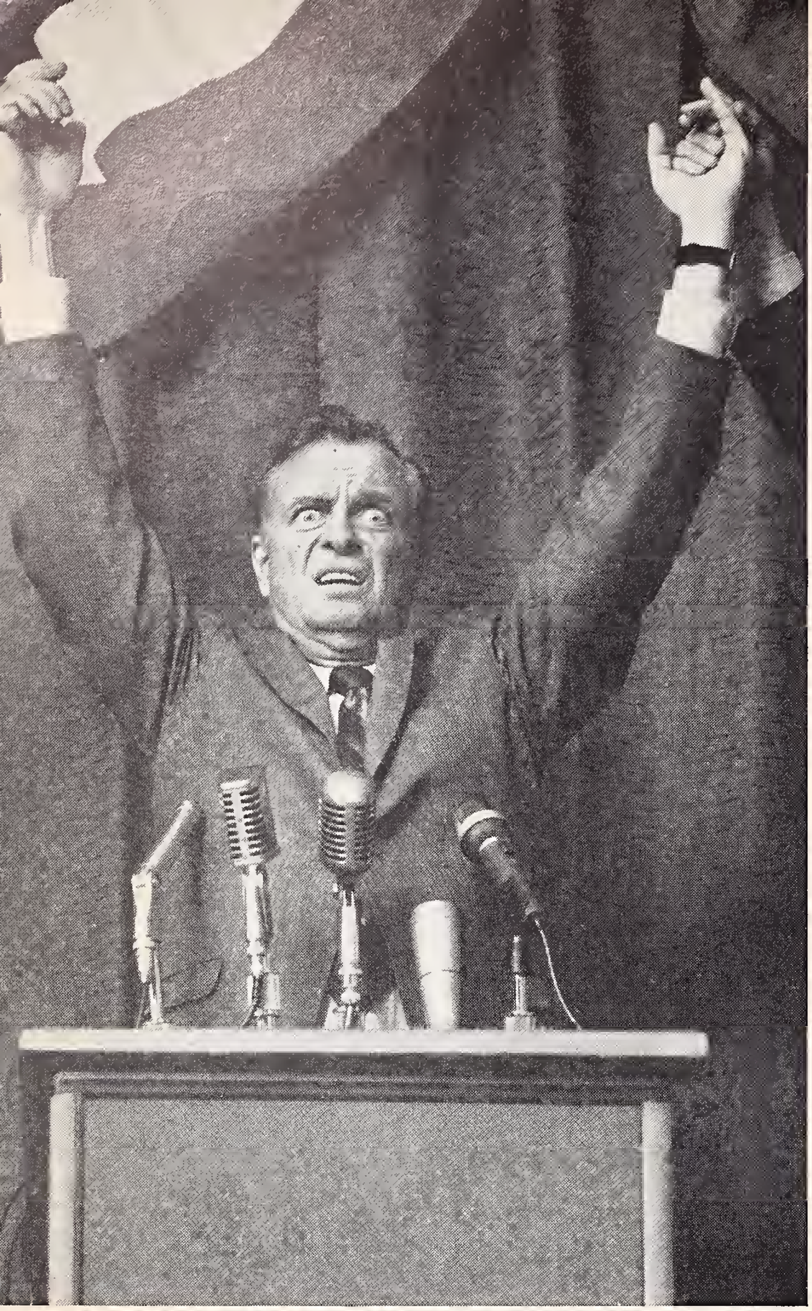
Also, in 1948, a private health insurance organization called the British United Provident Association (BUPA) began with 80,000 members. Today BUPA has income of more than 27 million dollars, and over 1.5 million members. More than half a million more Britains belong to other private health insurance plans. Recently BUPA has become an affiliate member of the National Association of Blue Shield Plans in the United States.

One of the supporters of socialism in Great Britain, Francis Williams, in his book "Socialist Britain," stated that "Here at last a practical test of two vast and so far unproven assumptions is taking place. The first is that a planned socialist system is economically more efficient than a private-enterprise capitalist system; the second is that within democratic socialist planning the individual can be given broader social justice, greater security, and more complete freedom than under capitalism."

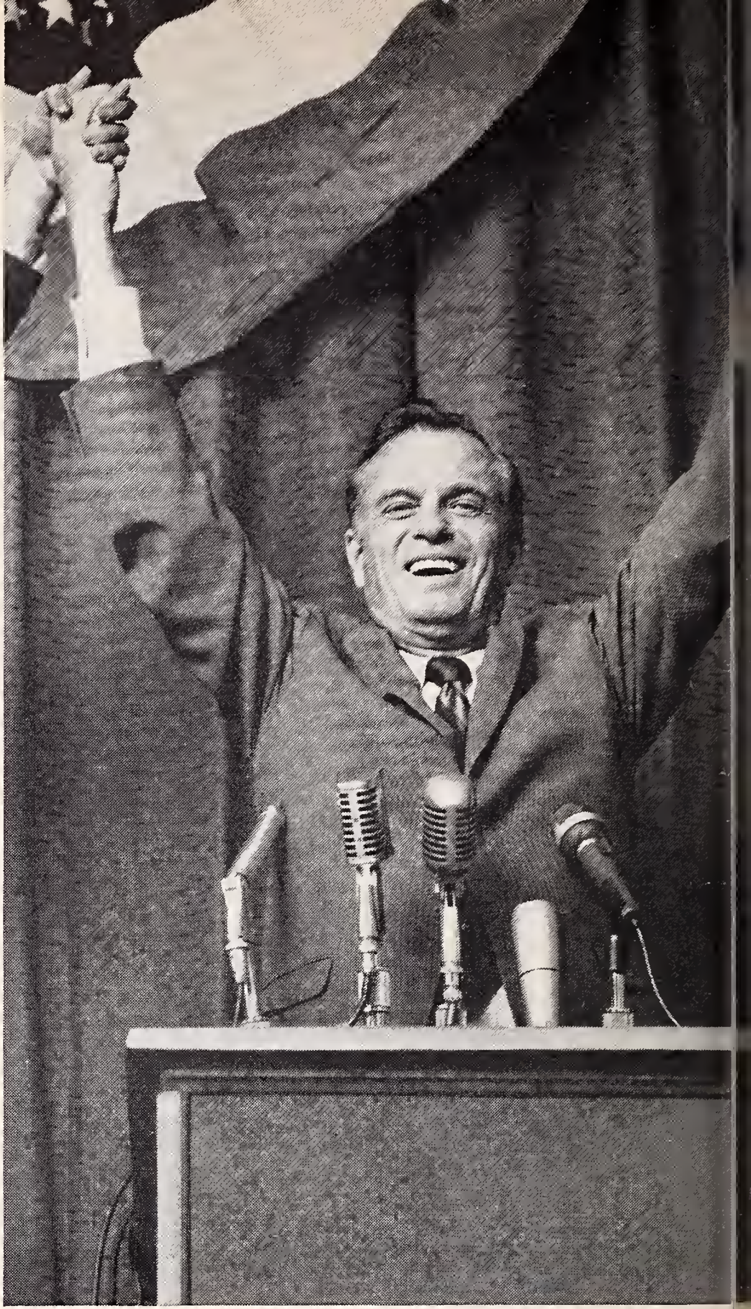
Perhaps such advocates who conceive socialism as a panacea to all problems have failed to admit even to themselves that the recipient of a service can claim it as a right only so long as the provider of the service can be coerced by the State into providing the service. Perhaps the Socialists also fail to remind the public that when the public has "the right" to treatment it abdicates "the right" to choose the provider of treatment.

Whether the "planned socialist system" of Williams has won the test against the "private enterprise capitalist system" in providing health care in England, I cannot say. Apparently over two million Englishmen think it has not.

Robert F. Lorenzen, M.D.
Editor



Picture of painful myositis



treated with Parafon Forte® TAB

Paraflex® (chlorzoxazone)* 250 mg.
Tylenol® (acetaminophen) 300 mg.

Parafon Forte tablets help to relieve pain, restore mobility...stop pain-spasm feedback by providing:

a nonsalicylate analgesic equal to aspirin for the relief of pain,[1,2] yet unlikely to produce the irritation to the gastric mucosa so often associated with salicylate therapy[3]

and a skeletal muscle relaxant shown to have up to a 6-hour span of action[4]...to retain effectiveness even on continued administration[4]...but not likely to have the central effects of tranquilizing compounds.[5]

Prescribe Parafon Forte for effective spasmolysis and analgesia in sprains, strains, myalgias, low back pain, bursitis and other musculoskeletal disorders. Your patients will appreciate the restored comfort and freedom of movement it usually provides.

Contraindications: Sensitivity to either component. ***Precauti***
Exercise caution in patients with known allergies or history
drug allergies. If a sensitivity reaction or signs or symptoms s
gestive of liver dysfunction are observed, the drug should
stopped. ***Adverse Reactions:*** Occasionally, drowsiness, dizzine
lightheadedness, malaise, overstimulation or gastrointesti
disturbances may be noted; rarely, allergic-type skin rash
petechiae, ecchymoses, angioneurotic edema or anaphylac
reactions. In rare instances, *Paraflex* (chlorzoxazone) may p
sibly have been associated with gastrointestinal bleeding. Wh
Paraflex (chlorzoxazone) and chlorzoxazone-containing pr
ucts have been suspected as being the cause of hepatic toxic
in approximately eighteen patients, it was not possible to st
that the dysfunction was or was not drug induced. ***Usual Ad***
Dosage: Two tablets q.i.d. ***Supplied:*** Scored, light green table
imprinted "McNEIL"—bottles of 100.

References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:
1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis
Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. R
J. L. A., *et al.*: Gastroenterology *44*:
1963. 4. Berman, H. H., *et al.*: Dis. N
Syst. *25*:430, 1964. 5. Friend, D. G.: C
Pharmacol. Ther. *5*:871, 1964.

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McNEIL LABORATORIES, INC., FT. WASHINGTON, PA. 19034

*U.S. PATENT NO. 2,895,

Painful night leg cramps...

unwelcome bedfellow for any patient—including those with arthritis, diabetes or PVD

One thing patients can sleep without, particularly patients with chronic disease conditions such as arthritis, diabetes or PVD, is painful night leg cramps. Although seldom the presenting complaint, night leg cramps can tie your patients up in painful knots. Now, just one tablet of QUINAMM at bedtime can usually bring an end to shattered sleep and needless suffering. Your patients will sleep restfully—gratefully—with QUINAMM, specific therapy to prevent painful night leg cramps.

Prescribing Information—Composition: Each white, beveled, compressed tablet contains: Quinine sulfate, 260 mg., Aminophylline, 195 mg. **Indications:** For the prevention and treatment of nocturnal and recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis and static foot deformities. **Contraindications:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions/Adverse Reactions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets.

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON-MERRELL INC.
PHILADELPHIA, PENNSYLVANIA 19144

Quinamm™ Specific therapy for night leg cramps
(quinine sulfate 260 mg., aminophylline 195 mg.)

Treating atrophic vaginitis complicated by infection… **is as easy as AVC/Dienestrol**

Dienestrol helps restore estrogen-deficient vaginal mucosa.
It is the *particular* ingredient in AVC/Dienestrol that improves cell maturation counts[1,2] — helps stimulate the restoration of normal vaginal epithelium to resist infection.

Two recent studies reconfirm AVC/Dienestrol efficacy.[1,2] AVC/Dienestrol is proven effective against monilial, trichomonal, nonspecific bacterial vaginitis, and mixed infections.[1,2] AVC/Dienestrol combats infection, helps restore tissue resistance to reinfection.

So even in complex cases, the treatment can remain the same. Comprehensive. Effective. Easy as AVC/D.

Contraindications: Known sensitivity to sulfonamides; diagnosis or familial history of carcinoma of the genital tract or breasts; precarcinomatous lesions of the vagina or vulva; palpable uterine fibromyoma; mammary fibroadenoma; depressed liver function.
Precautions/Adverse Reactions: The usual precautions for topical and systemic sulfonamides should be observed because of the possibility of absorption. Burning, increased local discomfort, skin rash, urticaria or other manifestations of sulfonamide toxicity or sensitivity are reasons to discontinue treatment. The use of AVC/Dienestrol does not preclude the necessity for careful diagnostic measures to eliminate the possibility of neoplasia of the vulva or vagina. Manifestations of excessive estrogenic stimulation through dienestrol absorption may occur. These include uterine bleeding, breast tenderness, exacerbation of menstrual irregularity and provocation of serious bleeding in women sterilized because of endometriosis. Endometrial withdrawal bleeding may occur if use is suddenly discontinued.
Dosage: One applicatorful or one suppository intravaginally once or twice daily.
Supplied: 'AVC/Dienestrol Cream'—Four ounce tube *with* applicator. 'AVC' and 'AVC/Dienestrol Suppositories'—Box of 12 *with* applicator.
References: (1) Salerno, L. J.; Ortiz, G., and Turkel, V.: Vaginitis: A Diagnostic and Therapeutic Approach, Scientific Exhibit, presented at the 115th Annual A.M.A. Convention, Chicago, Illinois, June 1966. (2) Nugent, F. B., and Myers, J. E.: Pennsylvania Med. 69:44, 1966.

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AVC/Dienestrol

Cream (dienestrol .01%, sulfanilamide 15.0%, aminacrine hydrochloride 0.2%, allantoin 2.0%)
Suppositories (dienestrol 0.70 mg., sulfanilamide 1.05 Gm., aminacrine hydrochloride 0.014 Gm., allantoin 0.14 Gm.)

One of these disposables comes prefilled.
Its unit dose – in nonreactive glass
cartridge – is premeasured.
The cartridge is clearly labeled:
drug name, strength, control number.
Even expiration date where appropriate.

You're more confident that the patient gets…

...just what the doctor ordered with the Tubex Closed Injection System.

Injections with the Tubex system are as easy as 1, 2, 3,

1. Select—from an extensive variety of prefilled Tube sterile cartridge-needle units.* No multi-dose vials to bother with; no unlabeled syringes to cause confusion

2. Inject—with a minimum of pain. Thanks to the single-use, stainless-steel needle that's both ultra-sharpened and siliconized. Aspirate simply and conveniently.

3. Throw away—empty cartridge-needle unit. Never used again, it can't transmit infection. And there's no clean-up job.

*For injectables not yet in the ever-expanding prefilled Tubex line, empty sterile cartridge-needle units are available.

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Closed Injection System
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Sterile Cartridge-Needle Unit

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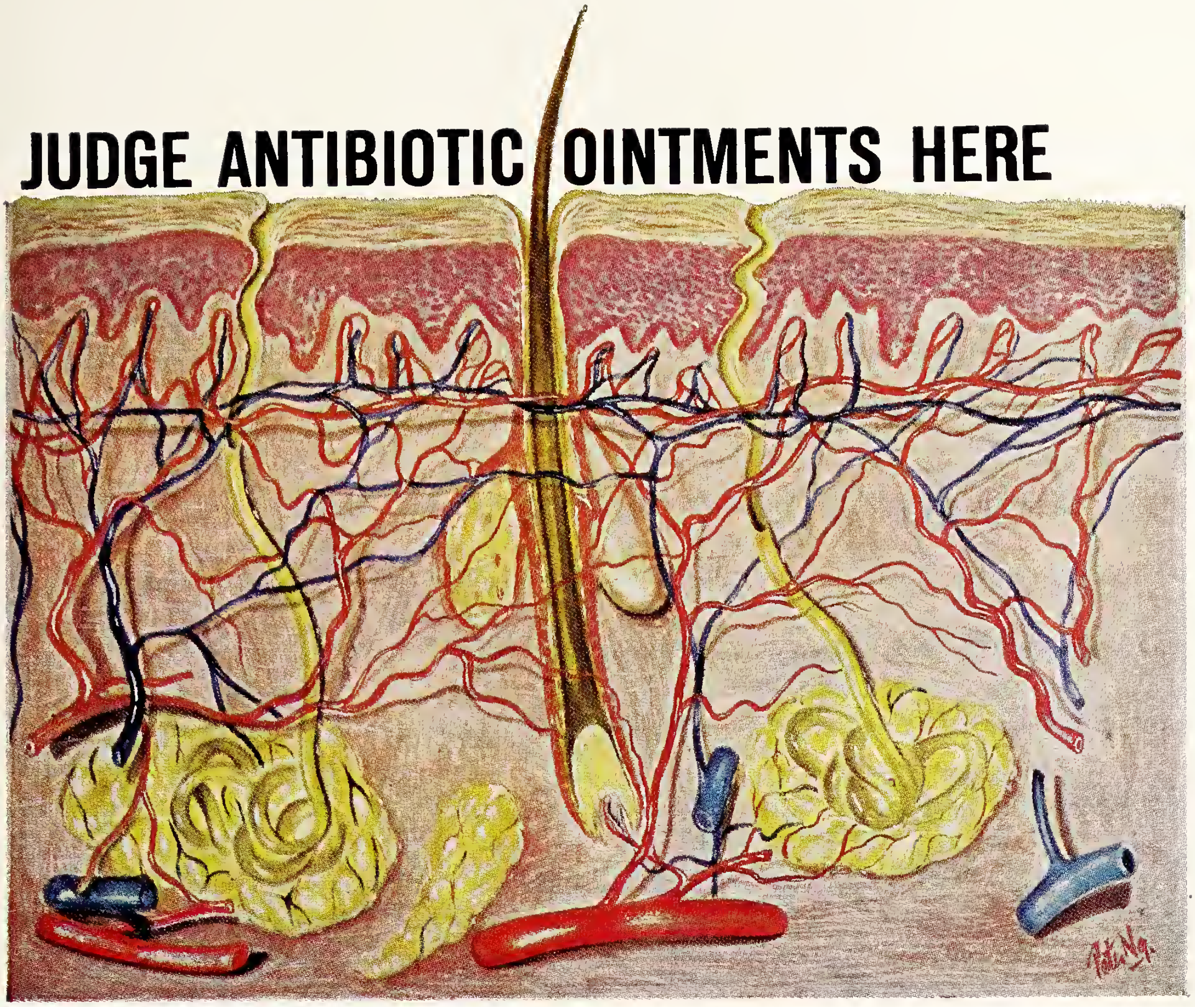

Results on skin are final proof of any topical antibiotic's effectiveness

No in vitro test can duplicate a clinical situation on living skin. 'Neosporin' (polymyxin B —bacitracin—neomycin) Ointment has consistently proven its effectiveness in thousands of cases of bacterial skin infection. The spectra of the three antibiotics overlap in such a way as to provide bactericidal action against most pathogenic bacteria likely to be found topically. Diffusion of the antibiotics from the special petrolatum base is rapid since they are insoluble in the petrolatum, but readily soluble in tissue fluids. The Ointment is bland and nonirritating.

Caution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.
Contraindications: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.
Supplied: Tubes of 1 oz., ½ oz. with applicator tip, and ⅛ oz. with ophthalmic tip.
Complete literature available on request from Professional Services Dept. PML.

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POLYMYXIN B-BACITRACIN-NEOMYCIN
OINTMENT

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N.Y.

No place for beginners

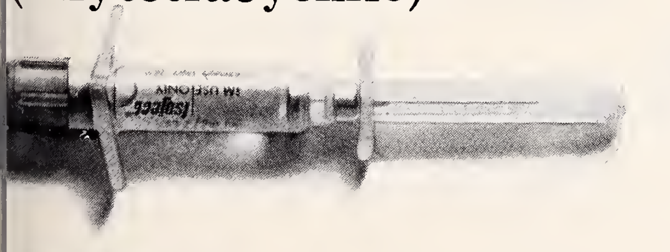
Terramycin®
(oxytetracycline)

Fire victim. Examination reveals second degree burn of lower leg. To combat shock, restore circulatory volume and replace protein loss, plasma is administered. Local pressure dressing applied. Limb elevated to limit the flow of lymph. About 36 hours after admission the patient develops an elevated temperature and complains of pain at the site of the lesion. Dressing removed. A suppurating slough area has developed over part of the burn. A swab specimen is taken for culture and the slough area is debrided. Antibacterial treatment is begun with Terramycin I.M. Days later, recovery is progressing, and the laboratory report shows a mixed infection with a predominance of susceptible coliform bacteria, confirming the therapeutic choice. Terramycin therapy is continued until all signs of infection disappear.

Experience has shown that Terramycin offers special advantages in treating bacterial infections complicating burns, when strains of causative organisms are susceptible. Broad-spectrum antibacterial coverage. Activity unaffected by penicillinase. Rapidly achieved therapeutic blood levels. Proven tissue toleration.

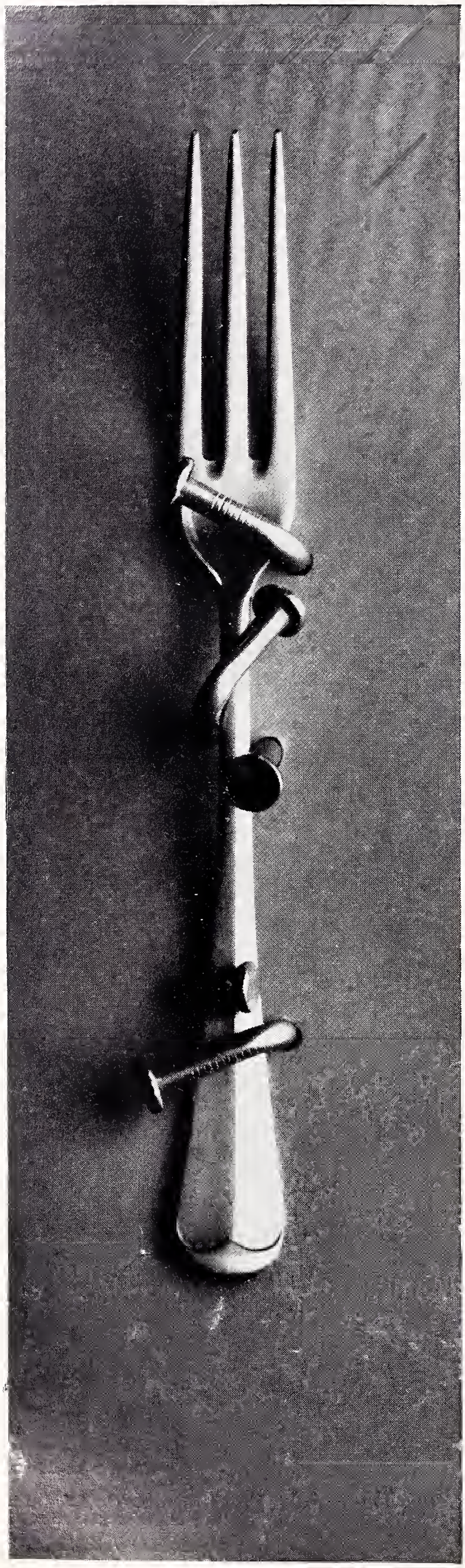
Terramycin I.M. is the only preconstituted broad-spectrum antibiotic designed specifically for intramuscular use. Requires no refrigeration. Remains stable for at least two years. Available for immediate use in Isoject,® a disposable injection unit. In difficult as well as routine cases, when tests reveal susceptible organisms, consider Terramycin. One of the world's most widely used broad-spectrums.

Terramycin® I.M.
(oxytetracycline)



Pfizer LABORATORIES DIVISION
New York, N.Y. 10017

Contraindicated: In individuals hypersensitive to any of the components of this drug.
Warnings: If renal impairment exists, even usual doses may lead to excessive systemic accumulation and possible liver toxicity. In such patients, lower than usual doses are indicated and for prolonged therapy oxytetracycline serum level determinations may be advisable.
Terramycin may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans.
Use of oxytetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of teeth. This effect occurs mostly during long-term use of the drug, but it has also been observed in usual short-treatment courses.
During treatment with tetracyclines, individuals susceptible to photodynamic reactions should avoid direct sunlight. Discontinue therapy at first evidence of skin discomfort.
Note: With oxytetracycline, phototoxicity is not believed to occur and photoallergy is very rare.
Precautions: Use of broad-spectrum antibiotics occasionally may result in overgrowth of nonsusceptible organisms. Where such infections occur, discontinue oxytetracycline and institute specific therapy.
As with all intramuscular preparations, Terramycin Intramuscular Solution should be injected well within the body of a relatively large muscle. *Adults:* The preferred sites are the upper outer quadrant of the buttock (i.e., gluteus maximus), or the mid-lateral thigh. *Children:* It is recommended that intramuscular injections be given preferably in the mid-lateral muscles of the thigh. In infants and small children the periphery of the upper outer quadrant of the gluteal region should be used only when necessary, such as in burn patients, in order to minimize the possibility of damage to the sciatic nerve.
The deltoid area should be used only if well developed such as in certain adults and older children, and then only with caution to avoid radial nerve injury. Intramuscular injections should not be made into the lower and mid-thirds of the upper arm. As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel.
Increased intracranial pressure with bulging fontanelles has been observed occasionally in infants receiving therapeutic doses of the drug, but such signs and symptoms have disappeared rapidly on cessation of treatment with no sequelae.
Adverse Reactions: Subcutaneous and fat-layer injection may produce mild pain and induration which may be relieved by an ice pack. Very mild gastrointestinal disturbances, not requiring discontinuance of the drug, may occur occasionally. Allergic reactions, including anaphylaxis, rarely have been observed.
Dosage: *Adult:* The optimal dosage varies, depending on the type and severity of infection. Unless otherwise specified, a dose of 100 mg. every 8 to 12 hours, or a single daily dose of 250 mg. should be adequate for the treatment of most mild or moderately severe infections. In severe infections, 100 mg. every 6 to 8 hours, or 250 mg. every 12 hours may be necessary.
Serum levels obtained by the recommended dosages are comparable to those provided by the oral dosage of 1 to 2 Gm. daily in adults. Antibiotic therapy should be continued for at least 24 to 48 hours after all symptoms and fever have subsided.
In certain diseases specific courses of therapy may be recommended as a general guide. In primary and secondary syphilis for example, the daily administration of 2 Gm. oxytetracycline, orally, in divided doses for two weeks has given good results. In cases of gonococcal infection two intramuscular injections of 250 mg. each, or one intramuscular injection of 250 mg. combined with one gram given orally as a single dose, will usually suffice, but repetition of this therapy will be required in an occasional case.
In the treatment of hemolytic streptococcal infections, therapy should continue for at least 10 days to prevent development of rheumatic fever or glomerulonephritis.
In the treatment of staphylococcal infections indicated surgical procedures should be carried out in all cases.
Pediatric: A dosage of 3 mg./lb./day in two doses has been found satisfactory in the treatment of most mild to moderately severe infections. For more severe infections, higher dosages may be indicated and should be adjusted accordingly.
Terramycin Intramuscular Solution provides maximum absorption and patient toleration with minimal local irritation.
Supply: Terramycin (oxytetracycline) Intramuscular Solution: available in single dose, prescored glass ampules containing 100 or 250 mg. oxytetracycline/2 cc., Isoject® syringes containing 100 or 250 mg. oxytetracycline/2 cc. and 10 cc. multiple dose vials containing 50 mg. oxytetracycline/cc.
More detailed professional information available on request.



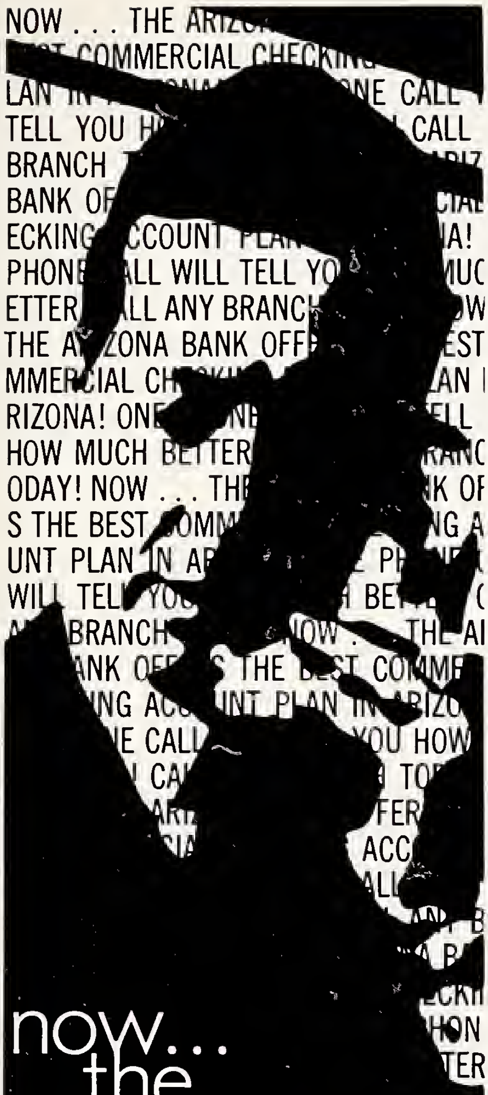
For the "Cheater Eater"

Formulas: Each 'Dexamyl' *Spansule* capsule No. 1 contains 10 mg. of Dexedrine® (brand of dextroamphetamine sulfate) and 1 gr. of amobarbital, derivative of barbituric acid (Warning, may be habit forming). Each 'Dexamyl' *Spansule* capsule No. 2 contains 15 mg. of Dexedrine (brand of dextroamphetamine sulfate) and 1½ gr. of amobarbital (Warning, may be habit forming).
Before prescribing, see complete prescribing information in SK&F literature or *PDR*.
Contraindications: Hyperexcitability, undue restlessness, hyperthyroidism, porphyria; in patients on MAO inhibitors.
Precautions: Use with caution in patients hypersensitive to sympathomimetics or barbiturates and in coronary or cardiovascular disease or severe hypertension. Excessive use of the amphetamines by unstable individuals may result in a psychological dependence. Rarely, symptoms of toxic psychosis (hallucinations, confusion, panic states, etc.) may occur with amphetamines, usually after prolonged high dosage. In these instances, withdraw the medication. Use cautiously in pregnant patients, especially in the first trimester.
Adverse Reactions: Overstimulation, restlessness, insomnia, g.i. disturbances, diarrhea, palpitation, tachycardia, elevated blood pressure, tremor, sweating, impotence and headache.
Supplied: In bottles of 50.

Dexamyl®
brand of dextroamphetamine sulfate and amobarbital
Spansule®
brand of sustained release capsules

curbs appetite
encourages normal activity
dispels diet discouragement

SK&F
Smith Kline & French Laboratories



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THE Arizona BANK
the bank that *makes* things happen...

Henry V, too,
suffered anorectal pain.

Henry V, hero of Agincourt, suffered severe anorectal pain due to a fistula in ano, for which the folk remedies and nostrums of the day provided little relief.[1]

Among the most common afflictions of man, anorectal disorders affect seven out of ten adults at some time during their lives.

1. Banov, L.: South. M. J. 57: 328-331 (March) 1964.

for symptomatic relief of initial inflammatory anorectal distress...

Anusol-HC®

hemorrhoidal suppositories with hydrocortisone

one suppository morning and evening for 3 to 6 days

Each Anusol-HC suppository contains bismuth subgallate, 2.25%; bismuth resorcin compound, 1.75%; benzyl benzoate, 1.2%; Peruvian balsam, 1.8%; zinc oxide, 11.0%; boric acid, 5.0%; and hydrocortisone acetate, 10 mg., plus the following inactive ingredients: bismuth subiodide, calcium phosphate, white wax and coloring in a cacao butter and hydrogenated vegetable oil base.

Precautions: Prolonged use of Anusol-HC might produce systemic corticosteroid effects. Symptomatic relief should not delay definitive diagnosis or treatment.

WARNER-CHILCOTT W|C MORRIS PLAINS N.J.

AN-GP-92

They don't feel they "suffer" from hypertension...

that's the "Buti" part of Butiserpazide.

The "Buti" part of BUTISERPAZIDE—the mildly sedative action of BUTISOL acting in concert with the classic thiazide/reserpine formula—proved helpful in one study in reducing hypertensive symptoms in over half the patients.[1]

Among the symptoms showing "striking" overall improvement were headache, nervousness, palpitation and dizziness. Nor is that all there is to the "beauty" of BUTISERPAZIDE. Clinical comparisons have also shown that many patients respond with smooth, uniform lowering of blood pressure[2]... at times *below* the levels achieved with previous therapy[1,2]... as well as a lowered incidence of drug side effects. (The usual dosage is just 1 tablet once or twice a day.)

You have a choice of 2 strengths:

Butiserpazide®-25

PRESTABS®* Tablets
BUTISOL® (butabarbital) 30 mg.†; hydrochlorothiazide 25 mg.; reserpine 0.1 mg.

Butiserpazide®-50

PRESTABS®* Tablets
BUTISOL® (butabarbital) 30 mg.†; hydrochlorothiazide 50 mg.; reserpine 0.1 mg.

Lowers blood pressure so smoothly that patients are often untroubled by either the disease...or therapy

*Warning: May be habit forming.

†15 mg. of BUTISOL (butabarbital), plus the other ingredients, in outer layer; 15 mg. of BUTISOL in a specially coated core for delayed release, to approximately equalize duration of action for all components.

Contraindications: Sensitivity to any component, porphyria, peptic ulcer, ulcerative colitis, mental depression, renal impairment or shutdown. **Warnings:** Consider the possibility of sensitivity reactions in patients with history of allergy or bronchial asthma. Coated potassium tablets, sometimes administered in conjunction with antihypertensive therapy, may be associated with small bowel lesions, which have led to obstruction, hemorrhage and perforation. Surgery has frequently been required and deaths have occurred. Such tablets should be used only when indicated and when adequate dietary supplementation is not practical. They should be discontinued immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occur. *Use in Pregnancy:* Exercise caution, since thiazides cross the placental barrier and may cause fetal or neonatal hyperbilirubinemia, thrombocytopenia or altered carbohydrate metabolism; adverse reactions seen in the adult may occur in the newborn. Use reserpine in women of childbearing age only when essential to patient welfare. Increased respiratory secretions, nasal congestion, cyanosis, and anorexia may occur in infants born to reserpine-treated mothers. **Precautions:** *Butisol* (butabarbital)—Exercise caution in moderate to severe hepatic disease. Elderly or debilitated patients may react with marked excitement or depression. *Hydrochlorothiazide*—May induce electrolyte imbalance; when used with digitalis or one of its glycosides and in patients with severe hepatic insufficiency, cardiac arrhythmias or symptoms of impending hepatic coma may occur. Discontinue and institute appropriate countermeasures if prolonged use produces hypokalemia or (likely with sodium restriction) hyponatremia and hypochloremic alkalosis. (Ammonium chloride, used to reverse hypochloremic alkalosis, is contraindicated in hepatic disease.) May produce elevated serum uric acid levels (and, infrequently, gout) or reduce glucose tolerance, altering insulin requirements in diabetics. *Reserpine*—Observe for signs or symptoms of peptic ulcer or ulcerative colitis. Discontinue at first sign of mental depression; keep in mind possibility of suicide. Exercise extreme caution in history of mental depression. May produce cardiac arrhythmias when used with digitalis and quinidine, or may precipitate biliary colic in patients with gallstones. Discontinue 1 to 2 weeks before surgery; inform the anesthetist in event of emergency surgery. Exercise caution in history of epilepsy. Discontinue 1 to 2 weeks before ECT. *General*—Exercise caution in coronary artery disease. **Adverse Reactions:** Dizziness, drowsiness, weakness, nasal congestion, leg cramps, nausea, palpitations, superficial skin bruises, palmar erythema, headache, dehydration, skin rash, "hangover," systemic disturbances, diarrhea, itching, vomiting, paresthesia, photosensitivity, pancreatitis, jaundice, xanthopsia, purpura, thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, anorexia, gastric irritation, abdominal cramping, constipation, glycosuria, vertigo, cutaneous vasculitis, orthostatic hypotension (potentiated by alcohol, barbiturates, or narcotics), increased salivation and gastric secretion, increased intestinal motility, loose stools, angina-like syndrome, arrhythmias, bradycardia, flushing, hypotension, nervousness, paradoxical anxiety, rarely atypical Parkinsonian syndrome, central nervous system sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, optic atrophy), dryness of mouth, syncope, epistaxis, weight gain, and impotence or decreased libido. **Usual Adult Dosage:** BUTISERPAZIDE®-25 or BUTISERPAZIDE®-50: 1 tablet daily or b.i.d. When used with other antihypertensive agents reduce dosage of both drugs about 50% and observe carefully for changes in blood pressure. *Before prescribing or administering, see package insert.* **References:** 1. Coodley, E. L.: Curr. Ther Res 4:460 (Sept.) 1962. 2. Johnson, H. J., Jr.: Penn. Med. J 67:35 (May) 1964.

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the inside story of a new antacid formulation...
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consistently scored high in degree and duration of intragastric buffering

Employing aspiration of gastric juice, indwelling electrode, and/or Heidelberg telemetering capsule techniques,* studies involving 79 subjects with or without proven peptic ulcer disease compared intragastric buffering capacity of Gelusil-M and 1 or the other or both of 2 leading ethical antacids, using comparable doses.*

All three antacids raised the pH above 3.5, an accepted criterion for antacids. The amount of time above this pH helps to characterize the buffering activity of an antacid. While it is not implied that a direct therapeutic correlation exists, these techniques do, however, objectively demonstrate the buffering characteristics of this new antacid in terms of onset of action, peak pH, duration of buffering action.

Mean peak pH*

Gelusil-M, mean peak pH 6.6 (range: 5.6-7.8).
Antacid A, mean peak pH 5.5 (range: 4.2-7.5).
Antacid B, mean peak pH 5.5 (range: 4.4-6.3).

Mean duration of buffering action above pH 3.5*

Gelusil-M, 29.8 mean minutes (range: 18.0-51.8 minutes).
Antacid A, 24.6 mean minutes (range: 6.3-48.0 minutes).
Antacid B, 23.3 mean minutes (range: 5.9-50.0 minutes).

Mean duration of buffering action above pH 5.0*

Gelusil-M, 23.2 mean minutes (range: 14.3-43.9 minutes).
Antacid A, 10.1 mean minutes (range: 6.7-12.2 minutes).
Antacid B, 16.3 mean minutes (range: 8.0-24.2 minutes).

Onset of action*

In speed of intragastric buffering action, Gelusil-M, Antacid A, and Antacid B were consistently rapid and not measurably different.

*References: Antacid studies, data on file, Warner-Chilcott Laboratories Division.

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GELUSIL®-M NEW

each 5 ml. teaspoonful contains:
500 mg. magnesium trisilicate, 250 mg. aluminum hydroxide (Warner-Chilcott), 200 mg. magnesium hydroxide
U.S. Patent No. 3,326,755

a consistent buffering anticostive† antacid

† Avoids constipation.

See next page for prescribing information ▶

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Gelusil®-M Liquid

Indications: Gelusil-M is indicated for prompt and dependable symptomatic relief of peptic ulcer, gastritis, heartburn, hiatal hernia, esophagitis, and other conditions for which control of gastric hyperacidity is required.

Precaution: Prolonged or intensive therapy in patients with severe renal insufficiency may lead to hypermagnesemia.

Dosage: One to two teaspoonfuls (5 ml. to 10 ml.) between meals and at bedtime or whenever symptoms occur. Certain conditions, such as acute peptic ulcer, may require individualized dosage. If diarrhea occurs, reduce dosage or discontinue use.

Supplied: Gelusil-M (spearmint-flavored)—light green bottles of 12 fl. oz.; and a **special hospital pack.** Keep tightly closed—shake vigorously.

Gelusil® Tablets

Easy to take along / easy to take / pleasantly mint-flavored. An antacid with adsorbent and demulcent properties which contains in one tablet: 0.25 Gm. aluminum hydroxide (Warner-Chilcott) and 0.5 Gm. magnesium trisilicate (USP).

Dosage: 2 tablets—or more—between meals and at bedtime, or whenever symptoms occur. Tablets should be chewed.

Regular Gelusil® Liquid

Pleasant mint flavor...ideal for hospital or home. Available in 12 fl. oz. and 6 fl. oz. bottles and a special hospital pack. An antacid which contains adsorbent and demulcent agents in each 4 ml. teaspoonful: 0.25 Gm. aluminum hydroxide (Warner-Chilcott), 0.5 Gm. magnesium trisilicate (USP).

Dosage: 2 teaspoonfuls (4 ml. each)—or more—between meals and at bedtime, or whenever symptoms occur.

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MENTAL HEALTH ....Mrs. Charles Conner (Ann)
4800 Valley Vista Lane, Scottsdale 85251
NOMINATING ....Mrs. Lewis S. Winter (Jean)
1714 East Rose Lane, Phoenix 85016
PARLIAMENTARIAN ......Mrs. Clare W. Johnson (Mary Ann)
318 W. Lawrence Rd., Phoenix 85013
PROGRAM ....Mrs. Evaristo Martinez (Frances)
1172 Country Club Dr., Prescott 86301
PUBLICATION ....Mrs. Philip E. Dew (Jean)
4112 East Fifth Street, Tucson 85711
Circulating Manager ....Mrs. T. Herman Moore (Teddy)
6402 Shepherd Hills Drive, Tucson 85710
SAFETY-DISASTER PREPAREDNESS:
Mrs. Charles I. Fisher (Peggy)
352 West Berridge Lane, Phoenix 85013
WA-SAMA ....Mrs. Ruben Acosta (Mary)
3481 E. Edgemont, Tucson 85716

ArMA Reports

THE MINUTES APPEARING IN THIS SECTION HAVE BEEN EDITED TO CONSERVE SPACE. A COMPLETE COPY OF THE MINUTES OF ANY MEETING WILL BE MAILED TO ANY MEMBER REQUESTING THEM.

BOARD OF DIRECTORS

Meeting of the Board of Directors of The Arizona Medical Association, Inc., held in the Convention Center of the Safari Hotel, Scottsdale, Arizona, Sunday, July 27, 1969, convened at 10:10 a.m., James L. Grobe, M.D., Vice President and Chairman, presiding.

MINUTES

Approved minutes of the meetings of the Board of Directors of this Association held April 22, 1969 and April 26, 1969.

ArMPAC BOARD OF DIRECTORS

Approved the appointment of Joseph B. DeLozier, M.D. and Mrs. Robert P. Mason, both of Phoenix; and the re-appointment of Walter Brazie, M.D. (Kingman, Chauncey D. Buster, M.D. (Yuma), Doyle Hansen, D.D.S. (Holbrook), Paul A. Hayes, D.D.S. (Phoenix), Ray P. Inscore, M.D. (Prescott), Mrs. Clare W. Johnson (Phoenix), John F. Kahle, M.D. (Flagstaff), Chairman, Paul W. Kliewer, M.D. (Wickenburg), Don V. Langston, M.D. (Phoenix), William W. McKinley, Jr., M.D. (Bisbee), Mrs. Robert J. Oliver (Tucson), William G. Payne, M.D. (Tempe), Eugene A. Savoie, D.D.S. (Tucson), William B. Steen, M.D. (Tucson), Sherman W. Thorpe, M.D. (Mesa), and Mrs. Lewis S. Winter (Phoenix), all as members of the Board of Directors of the Arizona Medical Political Action Committee, for the term of one year or until such time as their successors are appointed and have accepted office. Dr. Kahle reported by letter that all are agreeable to serving on the ArMPAC Board. It was determined that in the future, the ArMPAC chairman shall first present his recommendations to the ArMA Board of Directors for approval, and thereafter, each could be contacted for acceptance or rejection of appointment or re-appointment. It was directed this subject be included on the agenda of the next ArMA Board of Directors meeting.

ARIZONA REGIONAL MEDICAL PROGRAM

Locum Tenens Council

Discussed proposal of Dermont W. Melick, M.D. (Tucson) that there be established a Locum Tenens Council, the objective of which would be to canvass the physicians of Arizona with the hope that a goodly number of them will set aside certain specified blocks of time (two weeks to two months), during which time they would go to localities (in Arizona) of need and serve the citizens and/or hospitals in those local areas.

It was determined to approve the idea with enthusiasm; that the proposal be further explored to obtain more details; and that the president, Dr. Flynn, be authorized to confer further with Dr. Melick to explose the appropriate membership composite of an Ad Hoc Committee to undertake the study, which the President is hereby directed to appoint, having in mind that such committee might include, along with Dr. Melick, the President of each component county medical society or someone who would represent him, said committee to report back to the Board of Directors its findings and recommendations.

Sex Education

Numerous letters received from parents and others expressing disapproval of the introduction of sex education in Arizona schools taking the position that sex education is a family responsibility. Those letters received in time were forwarded to the ArMA Delegates and Alternates to the AMA House of Delegates. This subject was discussed at the Annual Convention of AMA in New York City recently. The following substitute resolution was adopted:

WHEREAS, the traditional sources of sex information and guidance for young people are often inadequate; and

WHEREAS, the local public and parochial schools — as social institutions accessible to all young people, reflecting broad community support and with sufficient intellectual and material resources — can aid substantially in the development of sound individual codes of sexual behavior; therefore be it

RESOLVED, that the American Medical Association recognizes that the primary responsibility for family life education is in the home, but that the AMA support in principle the inauguration by State Boards of Education or school districts, whichever is applicable, of a voluntary family life and sex education program at appropriate grade levels;

(1) as part of an overall health education program;
(2) presented in a manner commensurate with the maturation level of the students;
(3) following a professionally developed curriculum foreviewed by representative parents;
(4) including ample and continuing involvement of parents and other concerned members of the community;
(5) developed around a system of values defined and delineated by representatives comprising physicians, educators, the clergy and other appropriate groups; and
(6) utilizing classroom teachers and other professionals who have an aptitude for working with young people and who have received special training; and be it further

RESOLVED, that local organizations be urged to utilize physicians as consultants, advisors, and resource persons in the development and guidance of such curriculum and that state and county medical associations be urged to take an active role in this participation.

It was determined that those people making inquiry be informed of the AMA position regarding sex education; and advised the subject will be discussed at the next annual convention of this Association.

RMP Grant Application Endorsement

Dr. Flynn advised that following further review, he will report at the next meeting of the Board relating to grant application(s) endorsement associate with the Regional Medical Program.

ARIZONA HEALTH PLANNING AUTHORITY

Presidential nominations of the following board certified psychiatrists recommended by the Arizona Psychiatric Society submitted to the Governor June 6, 1969, to fill a vacancy within the Arizona Health Planning Authority, approved: Robert I. Cutts, M.D. (Tucson), Thomas F. Kruchek, M.D. (Phoenix), Robert C. Shapiro, M.D. (Phoenix) and Warren S. Williams, M.D. (Tucson). Dr. Kruchek was appointed by the Governor June 30, 1969, for the term ending February 1, 1972.

BOARD OF MEDICAL EXAMINERS — STATE OF ARIZONA

David D. Smith, M.D. (Flagstaff) appointed by the Governor a member of the Board of Medical Examiners of the State of Arizona for the term ending June 30, 1974. RECEIVED.

BENEVOLENT AND LOAN FUND COMMITTEE

Miss Patricia Anne Dixon (Tucson), by letter, expresses appreciation and thanks for scholarship grant awarded by this association. RECEIVED.

BUILDING COMMITTEE

Dr. Dew reported only 741 members have paid the full building assessment of $125.00, 639 members elected payment of $15.00 per year (total $150.00 over a ten year period), $86,645.00 was outstanding as of December 31, 1968, per audit, which has grown to $94,135.00 outstanding as of June 30, 1969. The initial estimated cost of the building was $220,000.00. The inflationary spiral resulting in increased cost of materials, labor, etc., was reflected in a contract award of $248,748.00 to the low bidder.

Authorized borrowing a sum up to $50,000.00.

EXECUTIVE COMMITTEE

Membership Classification Changes

Cochise

Max J. Kartchner, M.D. (Benson) Active granted Associate (Dues Exempt) account Residency Training, effective January 1, 1969.

Maricopa

Ira M. Bryant, M.D. (Mesa) granted Associate (Dues Exempt) account Retirement, effective March 1, 1969 (Board Action 4/22/69), further granted pro rata dues refund account illness from March 1, 1969.

Harold Pachtman, M.D. (Phoenix) Active granted Associate (Dues Exempt) account Residency Training, effective July 1, 1969.

Paul M. Mattson, M.D. (Scottsdale) Active Granted Associate (Dues Exempt) account Residency Training, effective July 1, 1969.

Financial Report

Accepted the report of the Treasurer covering the month of June, 1969. 'Income" $7,699.88 (total Income received — 1969 to date $206,840.30), reflecting an "under-budget" of $53,784.70 (1969 Budget $260,625.00). "Expenditures" $18,353.73 (total Expenditures 1969 to date $127,812.06), reflecting an "under-budget" of $132,812.94 (1969 Budget $260,625.00).

Approved supplemental appropriation requests:

500a Annual Meeting (Sch. II)	$4,840.74
(Net Deficit — Income over Expenditures — $409.44).	
500h Grievance	3.06
500v Resolution #6	28.70

Treasurer directed to revise 1969 Budget to hold expenditures within income.

ADJOURNED TO ENTER EXECUTIVE SESSION AT THIS POINT IN THE MEETING.

RECONVENED IN REGULAR SESSION.

In appreciation of outstanding loyalty and service, Bob Carpenter was presented with a three months paid vacation and round trip first class air fare to any place in the world.

INDUSTRIAL RELATIONS COMMITTEE

Industrial Commission of Arizona acknowledges receipt of listing of members comprising the Industrial Relations Committee of this Association for the fiscal year 1969-70, advising it will utilize its services if need arises. RECEIVED.

Walter V. Edwards, M.D., Medical Director, State Compensation Fund, expresses his view regarding the functions of the Industrial Relations Committee of ArMA and services rendered by it as a Medical Advisory Board to the Industrial Commission when called upon to so act. RECEIVED.

LEGISLATIVE COMMITTEE

Mr. Jacobson reviewed status of legislation proposed for introduction during the Second Regular Session of the 29th Arizona State Legislature suggesting strategy to achieve the objectives: (1) confidentiality of hospital records; (2) professional liability insurance measures in line with those introduced in California (five or six bills), three of which have been passed to date; (3) therapeutic abortion; and (4) privileged communication amendments. As regards consolidation of 90/10% licensing boards, the outgrowth of plans for state government reorganization, a special committee has been appointed, including counsel among its membership, who will study the problem and report to the Governor. More regarding this subject at a later date.

It was determined to support all of counsel's proposed actions relating to the subjects enumerated. Dr. Jarrett expressed the view that the professional liability insurance problem is extremely serious and he hoped priorities would be established listing this item number one in urgency.

The Board of Medical Examiners — State of Arizona requests its Executive Director be withdrawn from participation in legislative activities of this Association. So ordered, assigning this responsibility to Bruce E. Robinson, Assistant Executive Director, authorizing him to employ an associate executive director to assist him.

Dr. Henderson reviewed recommendations of the Legislative Committee in meeting held June 8, 1969, including some eighteen items relating to goals. Accepted report in principle.

MEDICAL ECONOMICS COMMITTEE

Supported the decision of the Medical Economics Committee to confer with the Industrial Commission of Arizona relating to the mounting objections of physicians involved in workmen's compensation cases regarding distribution of the new ICA insurance form; further supporting the introduction of legislative amendment, if found necessary, to achieve the relief sought.

Again approved the undertaking of a survey among those member doctors of medicine handling a major portion of workmen's compensation cases (Chapter 6, Laws of 1968) to ascertain their views and opinions regarding the operation.

Received for information, proposal of the Valley National Bank relating to self-employed Keogh Prototype retirement program plan.

Received for information, proposal of Charles Fisher, President, Armada Assurance Agency, Inc., suggesting creation by ArMA of its own H.R. 10 plan, he to serve as administrator.

Received for information, proposal of Charles Fisher offering through Hawaiian Insurance and Guaranty Company, Ltd., a deductible ($1,000.00-25% discount) $100,000/$300,000 professional liability insurance policy. It is considered the prerogative of Hawaiian should it elect to offer such deductible without the sanction of the Association. Dr. Cloud recognized certain pitfalls in any deductible insurance program and felt the membership should be fully apprised thereof when considering such program. Dr. Kennedy, speaking for Maricopa County Medical Society, expressed the feeling that ArMA rendered a disservice to its membership in recommending Hawaiian as an approved Association plan. It was pointed out that the Association had not endorsed the program, but rather approved its submission to the membership for individual consideration and evaluation. It was determined any deductible offering by Hawaiian made to individual members of the Association be made without ArMA approval in any way, subject to individual consideration and evaluation, and that surveillance of such offering by the Association be made as it proceeds. It was further directed that the Armada Agency be requested to submit to Staff any future mailings in advance thereof for review and approval; further, that through Medical Memos, relating to professional liability insurance, an article be inserted setting the membership straight as to ArMA's connection with Armada.

Truth in Lending

Bruce Robinson reported a further article will appear shortly in Medical Memos relating to the "Truth in Lending" statute which became effective July first last. The ArMA Delegates to AMA were instructed to present in resolution form, to be prepared by counsel and submitted to the Board of Directors at its September meeting for approval, for consideration of the AMA House of Delegates in Clinical Convention scheduled to meet in Denver, December next, deleting that portion of the law or regulation requiring compliance by physicians.

PROFESSIONAL COMMITTEE

Arizona State Hospital — Osteopaths

Willis H. Bower, M.D., Director, Arizona State Hospital, seeks the attitude, policy and action of this Association and its component societies should osteopathic physicians be employed by the Arizona State Hospital and admitted to membership on its medical staff. While the Board having referred this matter to its Professional Committee for study and recommendation awaits its report, it directed that a letter be forwarded to Dr. Bower stating that it would approve the hiring of well qualified, fully licensed physicians for positions in the state.

AMA — Osteopathy

Received from the American Medical Association policy statement adopted by its House of Delegates in 1968 Clinical Convention, together with guidelines relating to eligibility of qualified osteopaths for county and state medical society membership.

SCIENTIFIC ASSEMBLY COMMITTEE

Received report of John S. Turner and Associates regarding press, radio and television coverage during the 78th annual meeting of this Association held in Scottsdale, April 22-26, 1969.

Determined: (1) not to meet at Camelback Inn in 1971 because of lack of satisfactory arrangements; (2) to schedule the annual meeting of this Association in 1971 at the Safari Hotel, Scottsdale, April 27 through May 1; (3) to approve generally the proposed format of the 1970 meeting as presented which follows closely that of the 1969 annual meeting; (4) to approve the proposed 1970 schedule of registration fees reflecting a slight increase of $2.50 in certain categories, and establishing a fee of $25.00 for in-state non-members and $50.00 for out-of-state non-members; (5) to exempt military physicians from payment of registration fee only; (6) to continue the A. H. Robins Community Service Award; (7) to limit specialty group luncheon meetings to Tuesday through Saturday; (8) to again retain the services of John S. Turner and Associates in 1970; (9) to continue extending an invitation to those doctors of osteopathy wishing to attend the meeting; and (10) to recognize and approve the University of Oklahoma School of Medicine to conduct the scientific section program in 1971 or the University of California School of Medicine, Los Angeles.

COMMUNICATIONS

Student American Medical Association (Flossmoor, Illinois) expresses appreciation for ArMA's subscription—1969 Sustaining Membership. RECEIVED.

Merlin K. DuVal, M.D., Dean, College of Medicine, University of Arizona, expresses appreciation for AMA-ERF contribution of $8,259.19. RECEIVED.

Board of Medical Examiners — State of Arizona reports actions taken during its April meetings relating to Arizona licentiates. RECEIVED.

Woman's Auxiliary to the Arizona Medical Association expresses appreciation for allocation to it of $1,000.00 appropriation for 1970 activities. RECEIVED.

Approved without financial obligation its proposed program — "Work Week of Health" as being executed in Maricopa County, but to be sponsored by all county auxiliaries, the Maricopa County Medical Society, the Maricopa Mental Health Association, the Arizona State Nurses' Association, the state auxiliary, and other state organizations meeting board approval.

United States Pharmacopeial Convention, Inc., Nominating Committee, seeks nominees in the entire field of therapeutics to serve on election on the Revision Committee in the categories listed which "will make up the backbone of the U.S.P. Subcommittee on Scope for the 1970-80 decade." This committee will be responsible for selecting the drugs recognized in the two Pharmacopeias issuing in 1975 and 1980, respectively.

Determined: (1) to communicate with the Dean of the College of Medicine, University of Arizona, determining whether he would have any recommendations to ArMA as to possible nominees who would be interested in such assignment; and (2) to nominate Wallace A. Reed, M.D. to serve in the category of anesthetics.

OTHER BUSINESS

AMA 1969 Annual Convention

Dr. Cloud, Delegate to AMA, presented a resumé of the highlights of the AMA Annual Convention held in New York City, July 13 through 17, 1969. There were 196 items of business, 137 resolutions and 59 reports considered. The meeting convened Sunday afternoon with an impressive demonstration by the U. S. Drum and Bugle Corps. A medical psychiatric resident interrupted the meeting supported by quite a following of between 30 and 40 dissident medical students and their friends. A news release identified them as representatives of the Student Health Organization, the Medical Committee for Human Rights, the Movement for a Democratic Society, the Health Policy Advisory Center, the Rockefeller University Committee for a Democratic Society "and many others." The group's spokesman began by declaring the meeting "illegal and illegitimate" and ended by burning what he called his AMA membership card, but which television news described as a Blue Shield card. He came back Wednesday with a "non-negotiable demand" for 10 minutes to speak during the inaugural ceremony, but was flatly refused by the Reference Committee on Rules and Order of Business. A house resolution was introduced to consider non-hospitality in the future which was referred to the Board of Trustees.

The two resolutions introduced by the Arizona Delegation dealt with "smoking" and "removal of drugs from the market." The former No. 14 (A-69) was combined with two other similar resolutions introduced and combined in a substitute resolution, adopted as amended: "Resolved, that the House of Delegates of the American Medical Association actively participate in an anti-smoking campaign." The latter No. 15 (A-69) through considerable effort of the Delegate, was referred to the Board of Trustees and Council on Drugs for report at the forthcoming Clinical Convention December next.

The House resolved that AMA "should not attempt to establish a nationwide professional liability insurance program either by sponsorship of a program underwritten by an existing insurance carrier or by seeking to establish a new insurance carrier." It recommended that constituent associations: (1) "seek the enactment of appropriate state legislation designed to provide a more efficient and equitable determination of malpractice claims and litigation"; (2) that state associations, with the help of AMA, "seek the cooperation of hospital associations and third party payers in exploring and developing, if feasible, pilot programs which will provide scheduled benefits for persons injured as a consequence of medical accidents occurring in the delivery of health care, irrespective of fault"; and (3) "that workshops on malpractice insurance problems be conducted, as requested by the Board of Trustees, in which participation will be invited from (a) physicians confronted by insurance problems, (b) representatives of the insurance carriers, (c) staff attorneys of AMA and other appropriate staff personnel, (d) representatives and attorneys for the hospital service field, (e) nurses, and (f) legislators."

Amended the AMA Bylaws providing that "regular (AMA) membership shall be limited to those members of a state medical association who hold the degree of Doctor of Medicine or Bachelor of Medicine, or who hold an unrestricted license to practice medicine and surgery, and are entitled to exercise the rights of membership in their state medical associations, including the right to vote and hold office, as determined by their state medical associations."

Priorities on the AMA level were given to subjects including reasonable cost of health care, expansion of out-of-hospital health services, delivery of health services, medical manpower needs, sex education, health care for the poor, etc.

Discussion ensued regarding recruitment of medical corpsmen into the health personnel field under adequate surveillance, drug abuse, peer review, delivery of children by midwives, etc. Doctors Jarrett and Shapiro, Alternate Delegates, supplemented the report of the Delegate.

Reports of the Delegate and Alternate Delegates received.

Periodic Medical Relicensure

Approved appointments by the President to membership on the Ad Hoc Committee on Periodic Relicensure in accordance with ArMA House substitute resolution 10-69 adopted, including Drs. Jack M. Layton, Chairman (Tucson), Boyden L. Crouch (Phoenix), Arthur V. Dudley, Jr. (Tucson), Clifford J. Harris (Mesa), Paul B. Jarrett (Phoenix), Melvin W. Phillips (Prescott), and Robert E. T. Stark (Phoenix).

AMES Program

Dr. Schaller reported on the progress of the Air Medical Evacuation System to date. Operation is now under way. Sample cards were circulated designed to "calculate predictor value." It was determined to refer to the Professional Committee for review and recommendation as to approval of this basic system concept and report to the Board.

AMA Council on Mental Health

Concurred in the recommendation of the American Academy of General Practice nominating James L. Grobe, M.D. (Phoenix), Vice President of ArMA, to membership on the Council on Mental Health of the American Medical Association.

Board of Medical Examiners

Received notification submitted by the Board of Medical Examiners — State of Arizona listing officers elected for the fiscal year 1969-70: Otto L. Bendheim, M.D. (Phoenix), President; Deward G. Moody, M.D. (Nogales), 1st Vice President; Francis M. Findlay, M.D. (San Manuel), 2nd Vice President; Juan E. Fonseca, M.D. (Tucson), Secretary-Treasurer; David D. Smith, M.D. (Flagstaff), Member. Paul R. Boykin was appointed Executive Director of BOMEX for a similar period. Offices will continue to be located in Suite 101, Safari Building, 4601 North Scottsdale Road, Scottsdale — mailing address P. O. Drawer 1709, Zip Code 85252, to and including December 31, 1969. Effective January 1, 1970, it is the hope its address will be 810 West Bethany Home Road, Phoenix 85013, the new headquarters building of the Central Office of this Association.

Comprehensive Health Planning

No recommendation or action was forthcoming regarding the Second Conference on Comprehensive Health Planning Scheduled by the California Medical Education and Research Foundation, to be held at the San Marcos, Chandler, October 31 through November 2, 1969. Arizona is allotted fifteen (15) participants.

Registration fee $15.00. Grant obtained will provide lodging (2 in room) and meals. It was further reported that this meeting had been discussed with Stanford F. Farnsworth, M.D., Chairman of the Section on Comprehensive Health Planning of the Governmental Services Committee. In addition to himself, he has suggested that M. H. Goodwin, Jr., Ph.D., Director of the Arizona Health Planning Authority; Merlin DuVal, Jr., M.D., Dean, College of Medicine, University of Arizona; Milton Gan, Director, Comprehensive Health Planning Council of Maricopa County; George Rosenberg, Director, Comprehensive Health Planning Council of Pima County; and Dermont W. Melick, M.D., Coordinator, Regional Medical Program, be invited to participate. Wallace A. Reed, M.D., expressed an interest in attendance.

Hospital Expansion Monopoly —
Corporate Practice of Medicine

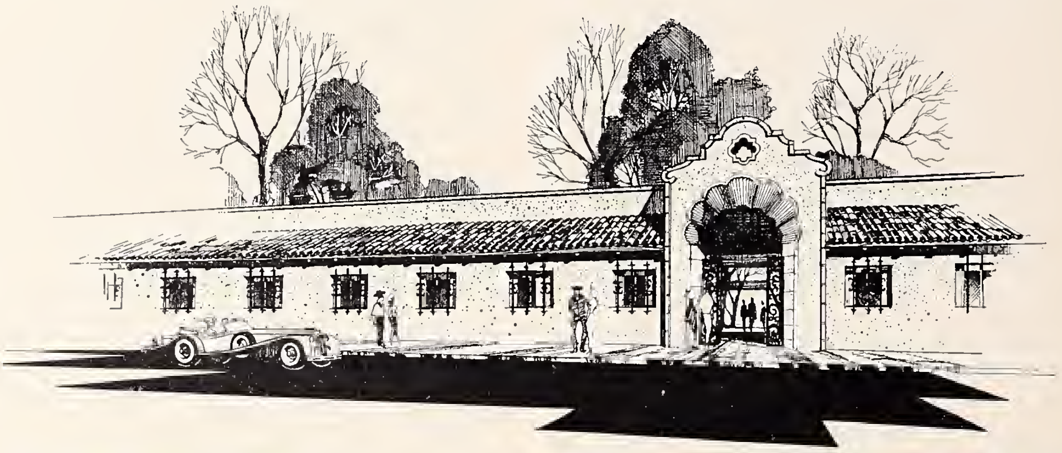
Gennaro Licosati, M.D. (Phoenix), President of American Academy of General Practice of Maricopa County, by letter dated July 22, 1969, expressed the concern of many physicians in this area referable to hospital expansion, the question of monopoly, and the question of the corporate practice of medicine. This latter one the Association is requested to explore.

The Executive Committee considered this subject at its meeting Saturday last recognizing emotions were involved, together with many factors known and unknown. Attention was directed to the Ad Hoc Committee to Study Hospital Based Physicians recently appointed by Blue Shield. Its membership includes: Clifton Alexander, M.D.; James Anderson, M.D.; William Bishop, M.D.; Harvey G. Brown, M.D., Chairman; Fred H. Landeen, M.D.; Robert Rehfeld; Nestor Roos, D.B.A.; James Thomas; Merlin K. DuVal, Jr., M.D.; Ray Leitner; William Dozer, M.D. It is recommended that this Ad Hoc Committee be utilized to obtain information and report back to this Board as soon as possible.

It was determined that the recommendation of the ArMA Executive Committee be implemented i.e. that the membership of the Blue Shield Ad Hoc Committee comprise an Ad Hoc Committee of this Association to Study the Practice of Medicine by Hospital Corporations, it being the thought that the proposed Blue Shield study authorized quite appropriately ties in with the study proposed by ArMA; that the function of the ArMA Committee will be to accumulate data relative to the subject and report back to its Board of Directors; and that Howard C. Lawrence, M.D. (Phoenix) and Walter Brazie, M.D. (Kingman) be also appointed and included in the membership of the ArMA committee.

MEETING ADJOURNED AT 3:15 P.M.

Edward Sattenspiel, M.D., Secretary
Robert Carpenter, Executive Director



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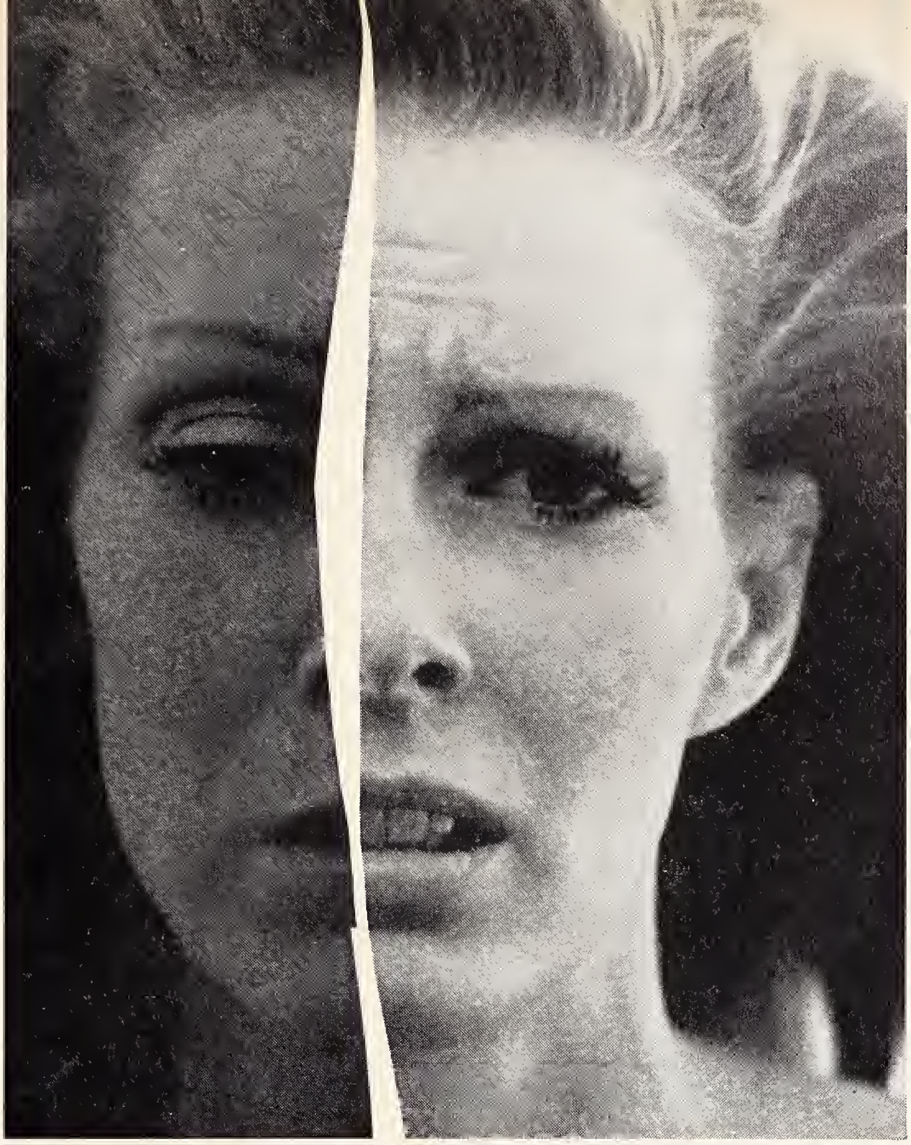

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Adverse Reactions: *Central Nervous System*—Drowsiness, especially with large doses, early in treatment; infrequently, pseudoparkinsonism and other extrapyramidal symptoms; nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. *Autonomic Nervous System*—Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. *Endocrine System*—Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. *Skin*—Dermatitis and skin eruptions of the urticarial type, photosensitivity. *Cardiovascular System*—Changes in the terminal portion of the electrocardiogram have been observed in some patients receiving the phenothiazine tranquilizers, including Mellaril (thioridazine). While there is no evidence at present that these changes are in any way precursors of any significant disturbance of cardiac rhythm, several sudden and unexpected deaths apparently due to cardiac arrest have occurred in patients previously showing electrocardiographic changes. The use of periodic electrocardiograms has been proposed but would appear to be of questionable value as a predictive device. *Other*—A single case described as parotid swelling.

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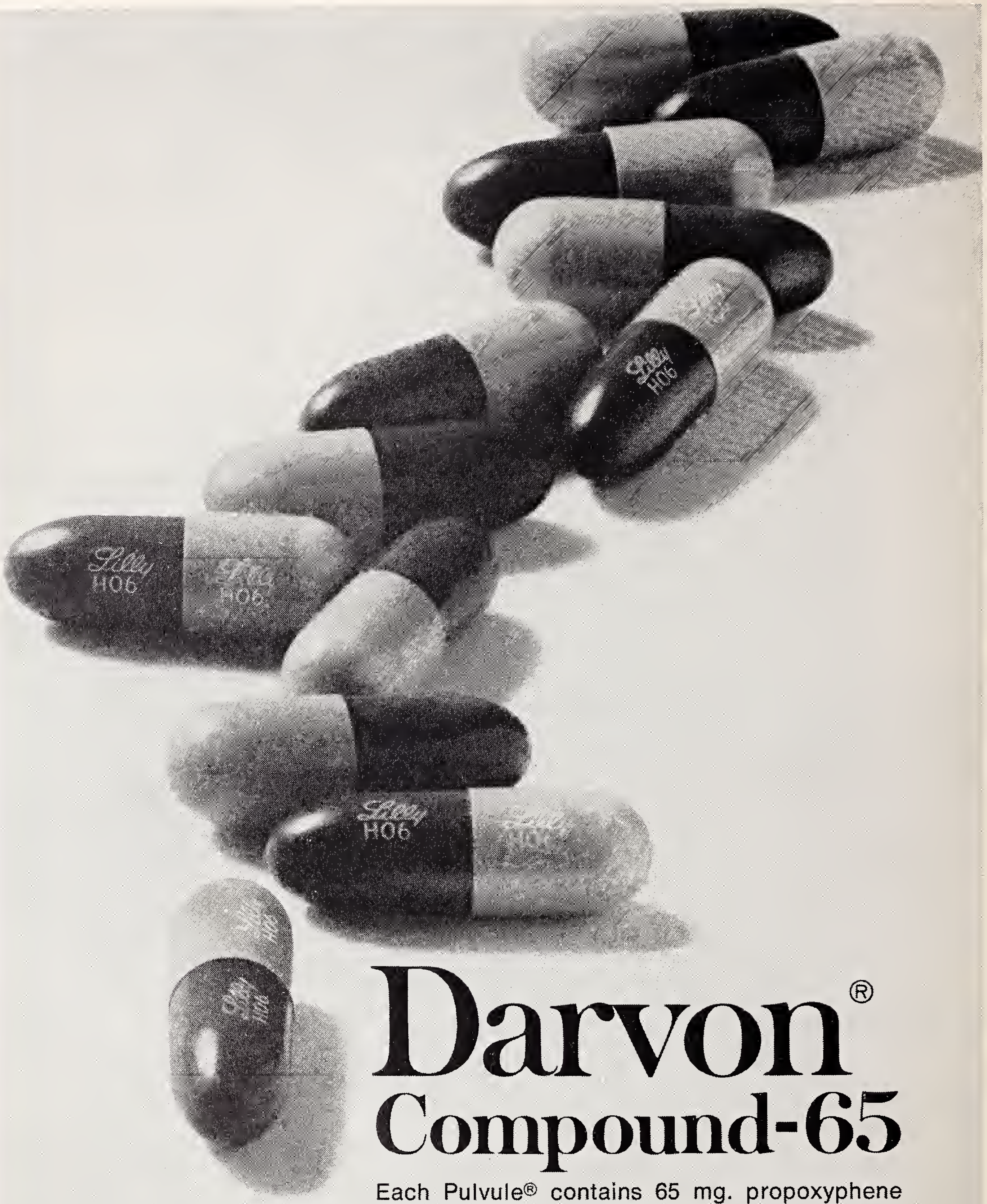

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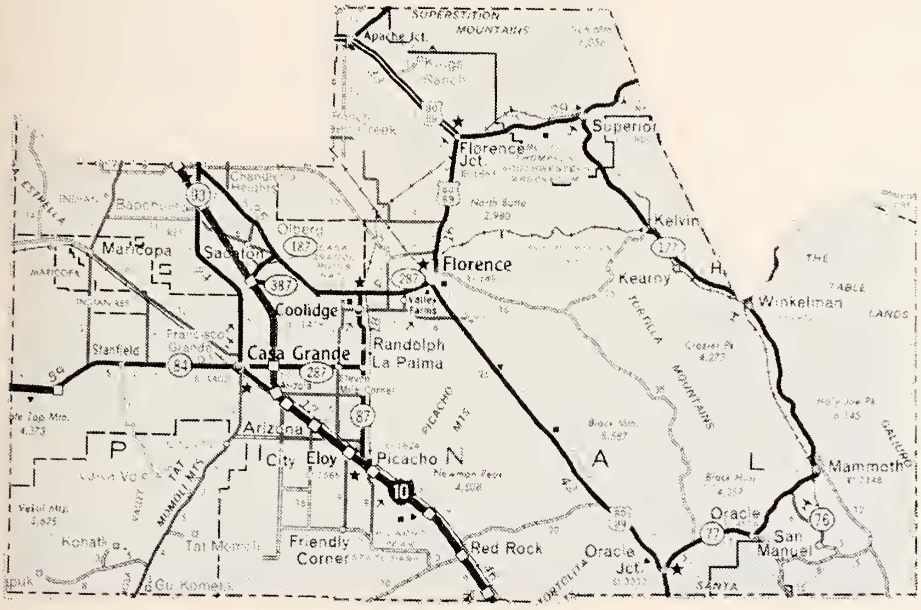
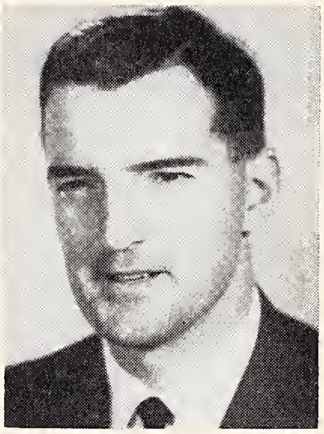


MENTAL HEALTH SERVICES IN PINAL COUNTY



Michael F. Cleary, M.D.
Director, Pinal County Mental Health Clinic

Development of mental health services in rural areas has not always kept abreast of urban facilities, and more particularly since the recent legislation in the community health field provided the impetus for a systematic expansion of mental health services on a nationwide basis.

In Arizona, mental health services have traditionally been concentrated in the two major metropolitan areas — Phoenix and Tucson. Until a few years ago, no psychiatric clinics functioned outside these cities, and mental health professionals were clustered in a similar manner.

Legislation in 1963 on the Federal level, known as the Mental Retardation Facilities and Community Mental Health Centers Construction Act of 1963, authorized Federal matching funds for a three-year period for use by states in constructing comprehensive community mental health centers. This was followed by similar legislation in 1965 authorizing matching funds for the staffing of these centers. The ultimate aim of these acts was the provision of adequate mental health services for each segment of the community; each community mental health center would be responsible for the provision of such services within a given catchment area, whose boundaries would be defined by geographic and population factors. A catchment area population should be between 75,000 and 200,000.

The regulations associated with the above legislation specified that five essential elements of service should be included — (A) in-patient services, (B) out-patient services, (C) partial hospitalization, including at least day-care, (D) emergency services provided 24 hours a day, and (E) consultation and education services. Additional services to be given when the comprehensive centers were fully developed included — diagnostic and evaluative services, rehabilitation, after-care, transitional and placement service, and community education activities.

This paper describes the development and progress of mental health services in Pinal County in 1968, with particular emphasis on two of the essential elements of service — out-patient services and consultation and educational services.

Pinal County, with a population of about 65,000, is slightly below the lower population limit for a catchment area; there is a concentration of population in the Casa Grande, Coolidge, Florence area; the smaller mining communities — Superior and San Manuel — in the eastern part of the county, account for most of the remainder. Treatment of psychiatric problems in the county in the past has relied heavily on the Arizona State Hospital in Phoenix, and on private psychiatric facilities and consultation in Phoenix and Tucson.

In 1967, the Division of Mental Health of the Arizona State Department of Health, through its Director, Dr. Ray Lewis, decided to make funds available for an out-patient psychiatric clinic in Pinal County, based on Florence, the county seat. The expense of staffing the clinic was underwritten by the Division of Mental Health with the hope that this initial effort would stimulate and encourage the leaders of the community to assume the economic and organizational burdens of the service at a later date.

The initial arrangement was that the clinic would be held, each Friday, at the county health department in Florence; this arrangement was later modified to enable clinics to be held at Casa Grande, San Manuel and Superior. Facilities for these clinics were provided by the Casa Grande Clinic and the Magma Company Hospitals at San Manuel and Superior. The activity of the clinic during 1968 can be divided into a number of phases. The early weeks were taken up with establishing the presence and identity of the clinic. Contact was made with possible major sources of referral within the county, in particular with the County Superintendent of Schools, the Superior Court, the Probation Office, welfare agencies, the Arizona State Hospital, and groups of clergy, teachers and family physicians. In addition, public health nurses, school psychologists, and organizers of such programs as Headstart Program and Grass Roots were contacted with a view to disseminating as widely as possible the information that this new service had begun in the county. Lines of communication were established with the 12-county unit and the Children's Unit at Arizona State Hospital; this was done to facilitate follow-up of patients discharged to the county from these units and to maintain contact with the treatment program of patients admitted to the hospital from the county.

The next phase consisted in provision of direct services to patients; this was limited to outpatient evaluation and treatment, with an occasional hospital consultation in the Pinal County Hospital. It was not possible to provide emergency or 24-hour service or screening. Each day of clinic operation has seen a full schedule. This was attributed to the preparation which consisted of meeting with the comunity agencies and leaders. Other results of these contacts included many follow-up requests for advice in handling of various problems, psychiatric, social, vocational and domestic, arising at various points within the county.

No restrictions on the category of patient by diagnosis, age or other consideration was imposed. This approach soon became reflected in the wide variety of patients referred, covering different age groups, occupations, ethnic groups and diagnostic categories. No distinction was made between child and adult patients. The terms of reference of the clinic were such that anyone with a psychiatric diagnosis or with a complaint which was thought by the referring person to be psychiatric in nature would be admitted, evaluated and treated. Because of manpower and financial considerations, it was not possible to embark on a comprehensive type of community mental health service; instead, the emphasis was on providing a service which would take first steps in surveying, evaluating and determining a disposition of the presenting problems.

From the beginning of the operation of the clinic, it was felt important to stimulate countywide interest in the maintenance of this service on a permanent basis. It became clear that the State Health Department, while providing initial operating funds, could not guarantee this support on an indefinite basis. Psychiatric outpatient clinics have traditionally had a wide base of community support; such resources as mental health associations, school boards, Boards of Supervisors, and organizations of interested citizens have usually been active and helpful. In Pinal County, the interest of unions and employers, service clubs and church groups and that of any other organization interested in the further development of mental health programs is sought and encouraged. The formation of a

Board of Directors and the incorporation of the Pinal County Mental Health Clinic in 1968 was a step toward placing the clinic on a firm and permanent footing. The need for services in the county has been amply demonstrated in the acceptance of the clinic during the year, the wide ranging sources of referral, the increasing caseload and the continued interest of community leaders.

Some major problems must now be faced, especially in the areas of financing and manpower. Indeed, manpower considerations have frustrated the development of total care in many areas; however, consultation and education may indirectly fill this need, at least in a partial sense. If the level of consultation is adequate and if communication or contact with professionals in the health field in general is maintained at all times, in-patient service and emergency service can be added. An appraisal of the county population should give an estimate of the number of mental health beds required to provide a minimum of adequate in-patient services. Such beds need not be in a formal inpatient psychiatric unit, but could be in rooms or sections of a hospital that can be modified or accommodated for the care of mentally ill patients. Provision of emergency services could be arranged through the hospitals which already provide emergency medical care and to which psychiatric care could be added by the provision of regularly available psychiatric consultation.

The Pinal County Mental Health Clinic now is essentially a private, non-profit health agency within the county, and can no longer count on support from any state agency. Although a sliding fee scale has been developed, and has been operative since October 1968, the income from fees will not pay for more than a small fraction of the expenses incurred by operation of the clinic. A general membership drive, aimed at all residents of the county, has invited participation by the public and some ideas for growth and development are being explored.

A tentative budget should include funds for professional and secretarial staff, and also for accommodation in the event that any of the agencies or facilities that have heretofore provided space are unable to do so in subsequent months or years. The mobile mental health clinic idea is recommended. This type of clinic has been used in other states and for the provision of other types of medical services such as TB screening, ophthalmological and obstetric clinics, dental clinics and clinics for general public health purposes. Descriptive material including brochures and films on the operating costs, maintenance and usefulness of such a mobile clinic is readily available.

It has been estimated by the National Institute of Mental Health that mental illness cost the country 20 billion dollars in 1967, the bulk of this going to the provision of treatment facilities, with the remainder attributed to loss of employment and other costs associated with mental illness. On a population comparison, the $20 billion figure for the nation would break down to a figure of $6 million for Pinal County. These figures demonstrate the dimension of the problem, and the hazard involved in ignoring, denying or minimizing its existence.

Table I outlines the number and location of clinics held during the year. Fifty-two clinics were held reflecting a total of 48 full clinic days. A portion of clinic time was spent in consultative activities with probation officers, school officials, clergy and welfare workers; this activity was in addition to consultation relative to individual patients, and represented a community information function of the clinic. This aspect was considered vital to further development, and especially crucial in the early stages of growth of the organization.

Table I
Total Mental Health Clinics Held and Location

Location	Number of Clinics	Full Clinic Days
Florence	34	32
Casa Grande	9	9
San Manuel	6	5½
Superior	3	1½
	52	48

Table II summarizes professional activity in the clinic in 1968; the professional staff consisted of the writer, in the capacity of psychiatrist and director, and William Luzader, ACSW, a social worker on loan from the Mental Health Division

Table II
Professional Activity — Pinal County Mental Health Clinic — 1968

Total number of patients seen	199	
Patient consultation (psychiatrist)	415	
Patient consultation (social worker)	106	
Total patient consultation	521	521
Consultation with persons other than patients, i.e. parents, probation officers, teachers, etc.,		
(a) psychiatrist	71	
(b) social worker	44	
	115	115
Total face-to-face consultation		636

of the Arizona State Department of Health, who was with the clinic for the first nine months of the year. At the close of the year, no psychiatric social work services were directly available to the clinic.

Table III describes some characteristics of the patient group seen in the clinic. Seventy-seven (38%) were 16 years or younger; another 53 (26%) were under age 30. The ethnic groupings seemed to be in proportion to the ethnic make-up of the county population. The chief sources of referral included the Arizona State Hospital, i.e. patients recently discharged from the hospital who are on conditional discharge, or who are still receiving medication or are being followed by the Hospital Community Representative in the county. Other major sources of referral included the county welfare office, the probation office, the public schools and the county health department.

Table III
Characteristics of Patient Group seen in Pinal County Mental Health Clinic — 1968 N. — 199

Age Groups		Ethnic Grouping	
0-16	77	White	130
17-30	53	Mexican-American	52
31-60	59	Negro	12
60 & over	10	Indian	4
	199	Other	1
			199

Source of Referral

Source of Referral	
Arizona State Hospital	29
Pinal County Welfare Department	28
Private Physicians	26
Probation Office	25
Public Schools	25
Pinal County Health Department	12
Family referrals	11
Clergy	5
Self-referral	5
Other	33
	199

Number of Patients Committed to Arizona State Hospital as a Percentage of Those Seen

Total number seen	199 (100%)
Committed	10 (5%)

It was necessary to commit ten patients from the clinic to the state hospital during the year. This amounted to 5% of the total number of patients seen. It is not possible to estimate at this time if the rate of commitment from Pinal County to the Arizona State Hospital was less in 1968 than in previous years or was in any way influenced by the operation of the mental health clinic. However, it is the impression of the staff that the rate of commitment was substantially lower, and that many patients who might otherwise have been committed were maintained on an out-patient basis. In the treatment and evaluation of former Arizona State Hospital patients who are on conditional discharge status, or who had formerly attended the Hospital Out-patient Clinic, the Mental Health Clinic staff co-ordinated their efforts with those of the Hospital Community Representative in the county. Not only has this avoided duplication of work, but it has helped to further the acceptance of the clinic by the many patients in the county who suffer from chronic mental illness. A possible extension to this joint effort that has been discussed is the visiting and treatment at home of the psychotic patient by a team consisting of the H.C.R. and professional clinic staff.

An additional service contracted for at the end of 1968, and scheduled to begin in January 1969, was the provision of psychiatric treatment, consultative and educational services to the Public Health Service Indian Hospital at Sacaton on the Gila River Indian Reservation; the initial contract for this service was drawn up between the Pinal County Mental Health Clinic and the U.S.P.H.S. office in Phoenix.

Comment

As the report indicates, the Pinal County Mental Health clinic has provided, during 1968, out-patient services and consultation and educational services within the community. Three other 'essential' items of service are missing; these are — in-patient service, partial hospitalization and emergency services. It is clear that in-patient and emergency services are vital if any service within the county is to earn the name comprehensive.

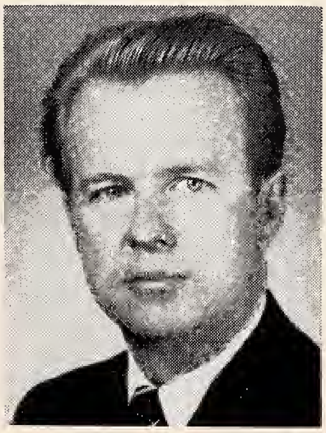
The initial funding of this project by the State Health Department represented an effort to encourage the community in the county to move in the direction of provision of total services.

The Pinal County Mental Health Clinic is a small, but significant beginning, and in the present form is easily capable of expansion. The expansion depends primarily on the support, encouragement and interest of the community. This type of support can be generated through the news media, through dissemination of information about mental health services, and by demonstrating the effectiveness of a properly organized and well-staffed clinic in handling psychiatric problems.

The second year of operation of the Pinal County Clinic has begun; it is hoped that this survey will be the forerunner of many others which will, as time goes on, reflect more comprehensive services.

THE ELUSIVE PROFILE OF THE TEENAGE DRUG USER

The initial psychiatric evaluations of 34 consecutive teenage referrals to a private psychiatric office were reviewed. Seventeen of the patients were drug users and seventeen were not. A multi-factoral psychosocial evaluation showed that there were no statistically significant factors which differentiated between the two groups, but some suggestive factors are noted. The author postulates that the primary determinants are social and cultural.



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The gravity of the teenage drug problem needs no elaboration. It has reached epidemic proportions, not only in the United States but in various other countries, and constitutes a major health problem.[1, 2, 3, 4, 23] The dangers involved in teenage drug use are both psychiatric,[5, 6, 7, 8, 9, 10, 12, 13, 14, 15, 16] and social (for example, the "Amotivational Syndrome").[17]

Some authors have attempted to correlate this phenomenon to cultural change,[18, 19] and more specifically to the so-called "hippie movement."[18, 19, 20, 21, 24]

There are relatively few reports in the literature which attempt to differentiate the teenage drug user from the non-drug user on the basis of psychosocial factors.[1, 16, 22, 23]

The purpose of this study is to determine what psychosocial factors might be regarded as significant in distinguishing the teenage drug user from the teenage non-drug user, and hopefully to define a psychosocial profile of the teenage drug user.

Methodology

The case material for this study consists of the initial psychiatric evaluations of thirty-four consecutive teenage (ages 12-19) referrals to a private psychiatric setting. All teenage referrals seen during a six-month period in 1968 were used in this study.

As no attempt was made to differentiate "experimenters" from habitual users, a drug user for the purpose of this study was arbitrarily defined as one who had occasion to use one of the following drugs during a three-month period prior to being seen: LSD, marijuana, STP, amphetamines, barbiturates, or other miscellaneous drugs such as solvents, mescaline, loco-weed, and "asthma cigarettes." None of the cases in this sample used "hard" narcotics.

As thus defined, seventeen of the thirty-four cases fell into the category of drug users, and seventeen did not. Eight of the drug users were male, nine female, and of the non-drug users, ten were male and seven female. The majority of all cases were of middle-class origin and average intelligence; the drug users and non-drug users were both quite homogeneous in these respects.

From the information in the initial psychiatric evaluation, each case was categorized by the author according to the following parameters:

1. Peer adjustment. Each case was rated good, fair, or poor.
2. Associated delinquency. The presence or absence of a history of other forms of delinquency, such as run away, incorrigibility, theft, etc. was noted.
3. "Broken home." This was defined as a home situation characterized by the absence of one or both natural parents.
4. Psychosexual maturity. Although all degrees of psychosexual immaturity were found in the sample, each case was rated as to the presence or absence of a severe disturbance in psychosexual development. Such a disturbance was usually characterized by confusion as to sexual identity, exceeding that ordinarily seen in adolescents.
5. "Hippie" philosophy. This variable was defined for purposes of this study as designating one who espouses, at least on a conscious level, the philosophy of the "hippies" as it is defined in our culture.[18, 19, 20, 24]
6. Predominant mood. All cases were rated according to predominant affect; three categories were used: (a) "normal affect," (b) anger, (c) major disturbance of affect — this latter category included either flattening or inappropriateness of affect of marked proportions.
7. Gross psychopathology. Four categories were employed: (a) neurotic, (b) adjustment reaction, characterized chiefly by rebellion against parents and authority, (c) schizoid, (d) pre-sociopathic. The latter designates adolescents who present primarily with normal affect, impulsivity, a hedonistic life style, and a general absence of guilt or remorse.

There were no psychotics or organic brain syndromes in this sample.

Results

1. Peer adjustment:

	Drug Users	Non-Drug Users
Poor	9	8
Fair	8	6
Good	0	3
P = 20%		

	Drug Users	Non-Drug Users
2. Other delinquent acts	11	8
No other delinquent acts	6	9

There is no statistically significant difference.

	Drug Users	Non-Drug Users
3. Broken homes	6	8
Intact homes	11	9

There is obviously a high percentage, greater than in the normal population, in both categories.

4. Psychosexual maturity:

	Drug Users	Non-Drug Users
Severely disturbed	5	6
Not severely disturbed	12	11

There is no statistically significant difference.

5. "Hippie" philosophy:

	Drug Users	Non-Drug Users
"Hippies"	6	2
Not "Hippies"	11	15

These findings are statistically significant to the 10% level, but this finding would be expected since drug use is one of the hallmarks of the "hippie" movement.

6. Predominant mood:

Normal	9	9
Anger	2	5
Major disturbance of affect	6	3

These results are not statistically significant.

7. Gross psychopathology:

Neurotic	2	4
Adjustment reaction	3	8
Schizoid	3	1
Pre-sociopathic	9	4

$P = 15\%$

These findings are suggestive, but not significant beyond the 15% level.

Conclusions

The findings in this study obviously fail to delineate any kind of specific psychosocial profile of the teenage drug user. But two of the factors studied warrant further comment.

That there is a preponderance of "hippies" in the drug-using group of teenagers comes as no surprise. The use of drugs is the manifest expression of the cultural change which has been described as the "hippie movement."

This study tends to provide some suggestive evidence of a correlation between early sociopathic manifestations and drug use. This finding, too, might be anticipated. It has been the opinion of this author that a large segment of the drug-using teenage population are basically delinquents, who, several years ago, would have presented to a psychiatric facility because of other forms of delinquency. It would appear that today, the use of drugs is the preferred form of delinquent expression. A few years ago, it might have been stealing cars, truancy, illegal possession of alcohol, etc.

In any case, it would appear that the treatment of drug users is approximately as difficult as the treatment of pre-drug era delinquents.

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President's Page

THE BOARD OF DIRECTORS

One of the hardest working groups of doctors in the Association is the Board of Directors. They meet every two months and run the Association, answerable only to the House of Delegates. Some of the problems that they face are exemplified by the meeting of July 27th. For the past two years, in an attempt to improve communications between the State and County Societies, the Presidents of all the County Societies, the Executive Secretaries of those Societies that have them, and the Executive Director of Blue Shield are invited to Board meetings. I think this approach has helped the communication problem somewhat. The first item on the agenda was a report from ARMPAC. About a third of the society are members of ARMPAC. This is good, but not as good as last year. The Board of Directors approves all members of the ARMPAC Board and this was done.

We received a letter from Dr. Melick on the formation of a Locum Tenens Council. The idea of the Council, a group of doctors who would be willing to go throughout the state to give relief to the local doctors for vacations or continued education, or to go to areas where there are no doctors now was approved with enthusiasm. A committee was authorized, made up of officers of all the local county societies to implement this idea. The Association makes recommentions to the Governor for many Boards and Commissions, and this falls on to the Board of Directors. Dr. Thomas Kruchek was nominated and appointed for a position on the Health Planning Authority, and Dr. David R. Smith was nominated and appointed by the Governor for the Board of Medical Examiners.

Authority was given to borrow up to $50,000 to complete the building (if everybody would pay their assessment in a lump sum of $125 rather than over the next 10 years, it wouldn't be necessary to borrow any money at all).

The Association has 13 standing committees, 5 ad hoc committees, and 23 sections of committees. These committees make recommendations to the Board, which has the authority and responsibility of putting these recommendations into action. It also has the honor of taking the blame if things don't go well. The Medical Economics Committee had met and recommended that an attempt be made to change the law requiring the physicians to send reports to the employers and insurance carrier rather than to the Industrial Commission. The Board approved this and instructed the Legislative Committee to implement this any way they could.

The Professional Committee received a request from the Arizona State Hospital asking their opinion on the employment of Doctors of Osteopathy. The Board felt that the state should hire any doctor who is well trained and qualified for the position open, and so informed the Administrator of the State Hospital.

The Scientific Assembly Committee has been busy, with a tentative program already set. They have arranged with the University of Texas Southwestern Medical School at Dallas to provide the faculty for the 1970 meeting, and University of Oklahoma School of Medicine for the 1971 meeting. John S. Turner & Associates were again given the job of publicity for the annual meeting. The U. S. Pharmacopeial asked for nominees for the committee on revision of the USP. This is just a preview of some of the actions of the Board at a slow summer meeting. The full actions of the Board are reported on page 710 in fine print, and I hope this has stimulated your curiosity enough to read them. The members of the Board listed on page 708 would really appreciate your comments on these or any problems that you may have. They are also in the best position to get Association support for any ideas or suggestions you might have. Talk to them.

Richard O. Flynn, M.D.

THE HORIZONS OF PEDIATRICS

What will the medical care of children be in 1980? in 2000? The answers to these questions are pertinent to the development of the Department of Pediatrics at the Medical College of the University of Arizona. We think the needs are clear. Physicians will be required to integrate genetic, biochemical and physiological information into the delivery of health care. For example, we now have the ability to "invade" the uterus and perform both diagnostic and therapeutic maneuvers on the developing fetus. We can also alter the expression of a few genetic diseases by dietary control. We employ electronic monitoring and environmental control in the newborn period. We treat bilirubin accumulation with phototherapy and drugs and have added "foot-candles" and "transducers" to our vocabulary. We interfere with normal immunologic responses by potent chemotherapeutic agents. We talk of mitochondrial respiration, of respiratory surfactant, of karyotype analysis and dermatiglyphics, of milliosmols and respiratory quotient, and so on. And not in the laboratory – but at the bedside and in the office. These were yesterday's horizons but they have rapidly become today's practice. Thus, in preparing for child care in the 80's and beyond, we must structure the education of the 70's to be in tune with anticipated therapy and practice; in other words, to train today's medical students in the thinking, the vocabulary and the practice of the future.

At the same time, we must also help the practitioner to readjust *his* thinking, vocabulary and practice so that it, too, will be in tune with the changing needs of practice. Thus, the major educational aim of the Department of Pediatrics is to provide an environment in which self-education of student, house-officer, faculty and practitioner is guided along paths appropriate to the future. The day of the "Ivory Tower" is gone – the medical college today must include the entire pediatric community in its educational endeavor.

At the same time that the University contributes educational know-how to the community it must reinforce the human elements in medicine. The practitioner and the faculty must both serve as models to the student, and must express concern with the health and welfare of each patient as a total person if we are to help the student develop an appropriate mixture of scientific humanity and humanistic science. Both will serve him well in the future care of children.

But education of the student and practitioner is not enough. The child population of our country is growing at a phenomenal rate – approximately 3.3% per year. It is anticipated that there will be 76 million children in 1980. The current ratio of pediatricians to children is approximately 1:10,000. When these figures are coupled with the observed decline in the number of general practitioners, it becomes painfully apparent that there simply will not be enough physicians to provide personal care for all of our children. In Pediatrics, this means the education, each year until the 1980's, of a number of pediatricians equal to the *entire* number of doctors graduated from all Medical schools each year – an obvious impossibility.

What can be done about this? What should the University do? We can: 1) produce more doctors; 2) expand the capabilities of each doctor; 3) develop new modes of patient care. We will continue to teach physicians how to make better use of their time in order that more patients are served. Thus, intelligent use of office personnel, community facilities, the telephone, printed instructions, technical procedures, counselling and other paramedical techniques will result in amplification of the physician's services to patients. In the past four years several programs have been developed which train non-M.D. health personnel who can meet some patient health needs. These programs have not yet reached the point where the qualifications, training and ultimate role of such individuals are certain. That they will augment medical care for children is clear, although how, and to what extent, they will fill the gap between need and availability of physician care is not clear. We will do our part to participate in the evaluation of the role of such persons in the delivery of quality health care to children.

In summary, the educational function of the Department of Pediatrics is two-fold; to develop quality of education and to increase the quantity of health personnel available to provide health care.

Editorial

UNREALITY OF RELATIONSHIPS

To be sane is to be in touch with reality. This is surely a minimum requirement. To be sane and healthy is to be an individual – in the literal meaning of the term, undivided – in transactions with reality. It is a matter of some concern.

A white-collar environment tends to keep us out of touch with reality. The successful man sits at his desk, pushes a button, speaks into a strainer of plastic and wire. He is a disembodied voice. His body, most of the time, is a useless, vestigial appendage of his brain.

Remember, up north, the Canadian geese flying in wedge formation across the path of the moon? They were calling to one another, needing friendship and reassurance for their ghostly journey. Those geese flew away with part of your soul!

The executive must be reminded when he is manipulating tokens and symbols. His stocks and bonds, his numbers and graphs, his little slips of paper, are a far cry from the hunks of raw material and the broken fingernails of labor which they represent.

Beyond the next ridge is a stand of aspen: comely maidens shaking their pagan tambourines.

When an officer sends a battalion into combat or an industrialist orders a lay-off, he can hardly feel responsibility or solicitude for each and every individual affected by his decision. By being impersonal he is obviously less than a complete person.

Before daybreak it will begin to snow, softly, unhurriedly, flakes the size of potato chips. Then you will hear the ululating song of the coyotes.

As we function more and more at cortical levels, levels of abstraction and generalization, so we get further from reality. Instead of dealing with persons and things as they are, we become occupied in and with relationships. And we treat them as if they were real.

Relationships are by definition reciprocal: husband-wife, boss-secretary, doctor-patient, salesman-customer, landlord-tenant. It is like two sweating clowns under the costume of a horse. Without realizing it we become enmeshed in these relationships, these contrived, artificial roles and incomplete identities.

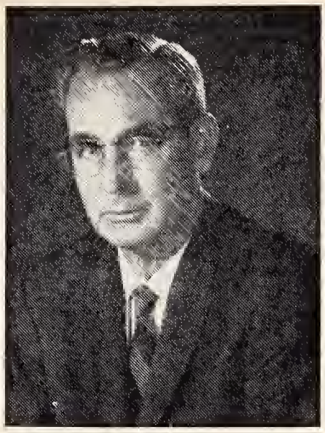
You can translate the worrisome conversation of the quail, running to hide like naughty children, warning the approach of the grown-ups.

We are reluctant to change relationships or to mix them. Is this not true? One hesitates to pay a compliment or volunteer a favor to a powerful associate lest it be interpreted as flattery or a bribe. Is it not awkward, for another example, for a woman to be both a doctor's wife and a patient? Or, the old question, can a physician ever really be an intimate friend?

No; not quite. Anyone with that degree of objectivity or maturity or self assurance would probably repel the rest of us who are still so insecure and sensitive.

The cue stick couples with the willing chalk. Could any still life be prettier than a pool table with all the balls neatly racked? Celestial spheres or an early model of the atom?

Any significant relationship implies some mutual dependency, some obligation on either side. And this, of course, entails the likelihood of being disappointed or – more painfully – of being a disappointment. Hence every relationship leads to some secretiveness and ambivalence, some readiness for guilt or anger. Any uniform, psychic or otherwise, will partially stifle affection and humor and honesty.



William B. McGrath, M.D.

Surely the oldest and richest scent of all is that of baking bread. I like the clean smell of lumber, maybe because my dad was in the lumber business. He read to us the tales of King Arthur, and he had a baritone voice like fine leather.

To be more self contained is to be constantly mindful that relationships are without dimension or substance. In the last analysis they are nothing more than products of our imagination. They are simply not real.

Yet it would take an impossible leap of the spirit to get out of these nets which will not let one be one's self. One could still carry the same responsibilities, and not unwillingly. But at least during interludes of leisure he might be rid of the indescribable nervous dissatisfaction of feeling divided and incomplete.

Above the lobby of that elegant old hotel there is a mezzanine. You should sit there and write funny-serious letters to the children of your friends. They want to be friends of yours, too.

In any acquired identity or in any given relationship (husband, father, wage-earner) a person may trudge in the miserable bleakness of failure or he may be most grievously hurt. If he cannot harden his heart, where can he turn?

Instinctively we turn to nature. In the absolute simplicity of natural surroundings a man can recapture the organic feeling of wholeness. This is because in nature we are back in touch with reality. Stripped of guardedness and role playing we can be truly close to one another. And in spite of our analytic intelligence we can be innocent and wholly alive.

When spring comes again the ice in the river will break and melt, and then we can go home.

"CODAC"

It has been a little over two years that the Maricopa County Medical Society's Drug Abuse Committee flexed its collective muscle and entered the lists in the battle to curb drug abuse among our younger generation.

It was an awesome challenge then — and even greater responsibility today. Surveys, studies and statistics are in general agreement that between 25 to 35 per cent of our Valley's school age population have or are using marijuana and/or other drugs and narcotics.

Add this to your non-school, or drop-out population, and it becomes evident — shockingly evident — that we are talking about 12,000 to 15,000 youngsters and nearly as many frightened families.

The problem has tremendous dimensions. Understandably, its solution calls for bold approaches of equal magnitude. Talks to school-age children and concerned adult groups . . . film showings . . . panel discussions on broadcast media . . . literature distribution . . . publication of material in print media . . . seminars . . . workshops . . . *all* are vital weapons in the fight against drug pollution. But they *cannot* win the battle — collectively or individually. Ultimate victory demands even more.

If we are going to cut down the drug problem to a size we can handle, we must involve far more teenagers on our side . . . we must provide treatment and therapy centers for young people wanting to rid themselves of the drug habit . . . we must enlist the support of more civic groups, of appropriate governmental agencies, of religious bodies and as much of the business community as possible.

So widespread, so costly, so all-pervading is the drug problem that it calls for nothing less than total, coordinated commitment!

Ever since "Dope Stop" was launched by the Maricopa Mental Health Association in early February of this year, the Maricopa County Medical Society, via the Drug Abuse Committee, has been working shoulder-to-shoulder with it. We accepted responsibility, for example, for the preparation of a weekly series of pertinent questions and answers dealing with drug use and abuse. This feature has been appearing in the Saturday Teen Gazette section of the Phoenix Gazette, the Association's "Health Tips," as well as other print media, radio and television.

"Dope Stop" also has generated numerous appeals from young drug addicts seeking medical help. To protect confidences to the hilt, only cursory records have been kept but a conservative estimate is that we collectively have counseled and treated many young men and women over and above those encountered in our regular practice . . . these were in all age ranges. And, collectively, as many personal inquiries from users and parents have been answered by letter or telephone. How many youngsters, young adults and mature men and women have been convinced, directly or indirectly, that the use of drugs is a questionable pleasure at best and a deadly one at worst — we'll never know . . . their number may not be legion, but surely it is substantial.

Involvement of organizations dealing with drug use and abuse was the next step . . . out of this we have established . . . "Communitywide Organization for Drug Abuse Control" or "CODAC" . . . from the cooperative efforts of the concerned resources of the community which included, State, County and City organizations. Within the framework of that overall coordinating body, work will continue on various levels, in addition to the all-important work of helping to make short-term treatment and therapy facilities a reality as quickly as possible.

Much is left to be done, although the first hurdle has been surmounted, such as procuring a contact center for young drug abusers who are seeking help. The center staffed by former users and a counselor provides a central location for those who need to seek help. Although no medications are administered at this facility, it is a referral point to more comprehensive care according to the need.

The young staff members, having formerly been of the drug society, are apprised of the problems facing a youth in trouble and can be instrumental in bridging the communication gap.

This is but the first of 3 proposed facilities projected by the CODAC Committee. In addition to the contact point there is a need for a hospital facility specifically for the drug abuser. Add to that a Rehabilitation center for detention without contamination. This would detain some of the young offenders now out on probation.

We hope that Arizona physicians will answer our call for financial help in a manner that brings honor to the healing profession, only then can these facilities become a reality as quickly as possible.

OUR NEW HEADQUARTERS

AS OF
JULY 14TH

After carefully reviewing the bids presented by seven contracting firms, the Ad Hoc Building Committee voted to award the contract to build our new headquarters to Gilbert and Dolan Construction Co. of Phoenix, Arizona. The contract was reviewed by our legal counsel, Mr. Edward Jacobson, approved, and was then signed formally with representatives of Gilbert and Dolan.

Shortly thereafter the project was begun. Excavation of the basement level was the first order of construction. As the basement will be a full floor, considerable excavation was necessary. On its completion, the foundations for the walls and pillars of the entrance area were prepared, concrete poured, support columns raised, and the block walls for the lower floor were added. This is the current status of the construction project.

The building committee approved this basement floor for our future needs. All current requirements will be met in the second or ground floor. However, the relative cost of this basement is so low that we decided to add it at this time. It will not be completed or furnished during our current building program, but it will be ready for any future expansion that your State medical association may need. At the rate building costs are advancing, this section can be erected now for a much smaller amount than will be the case in another 5 or 10 years. It was the conviction of the building committee that this plan would be much more economical for us in the long run. Accordingly, this basement floor is in our current program.

Gilbert and Dolan have a contract which calls for completion of the project within 135 days. Therefore, if no unforeseen strike or material shortage develops, we can expect completion of our new quarters by December 15th.

Robert A. Price, M.D.
Chairman, Ad Hoc
Building Committee

AS OF
JULY 29TH

U of A RECEIVES $502,845 TO OPERATE NEIGHBORHOOD HEALTH CENTER

The University of Arizona has received a $502,845 grant to develop and operate a neighborhood health center in Tucson.

The Department of Community Medicine in the College of Medicine received the federal funds to provide a comprehensive medical care program in the Model Cities area.

The grant, announced by Sen. Paul Fannin, is from the Community Health Service and Mental Health Administration, Department of Health, Education and Welfare. The grant covers the first of a scheduled five-year program. No state funds will be involved in the federally-financed program.

Dr. Herbert K. Abrams, professor and head of the Community Medicine Department, said the aim of the program is to provide high quality medical care which will be developed as a service to the community and as a resource for the College of Medicine. The program has been designed to serve a population of approximately 10,000, including about 3,500 entitled to care at the county hospital.

The Pima County Board of Supervisors has

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PROGRAM OF COMMUNITY MEDICINE AT THE UNIVERSITY OF ARIZONA COLLEGE OF MEDICINE

Herbert K. Abrams, M.D.

The concept of community medicine is not new. It is simply a re-discovery of old principles. Community medicine is concerned with the relationship of individual health with the environment; the distribution of medical care in the community, and epidemiology, the science of the behavior of disease and health.

Translated into medical education, community medicine is concerned with the problem of how to maintain relevance between the product of the medical school and the needs of society.

Since the Flexner Report of 1910, the trend in medical education has been toward ever greater specialization with consequent fragmentation of medical care and diminution of the prestige and the numbers of general and family practitioners. (One interesting result is that today we actually have fewer physicians per 100,000 population than we did in 1900.) During the same period there has been a great proliferation of paramedical specialties so that the individual physician has become increasingly dependent upon many other skills.

Simultaneous with this trend has been the industrialization and urbanization of the populaalready indicated that the health center can be located in the former juvenile detention home near Congress St. and the Freeway.

"We will develop a close working relationship with the residents of the area. The center will be closely integrated with planning for the Model Cities Program and with other health and social agencies. It will employ and train community residents as family health workers and for other skills," Abrams said.

The center, which will operate as an outpatient clinic, will relieve some of the burden on the County Hospital. Eligibility for care will be based on residence in the Model Cities area and financial ability to pay for services, he explained.

The center will be staffed by physicians from the College of Medicine, including Tucson doctors employed to assist in the program. The Department of Community Medicine will operate the center. The Colleges of Nursing and Pharmacy will staff and operate services in their respective areas, Abrams noted.

He emphasized that "responsibility of medical care will be in the hands of fully qualified physicians. Students will be involved in a learning capacity. The objective from the point of view of students is to train them to become family and community oriented physicians."

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tion. One result of this process has been the development of huge poverty ghettoes in all of our cities. This has caused strain, dislocation and inequity in our mechanisms for the delivery of medical care. Yet most medical schools, with the inertia of big institutions, continue to educate within the framework of teaching hospitals and specialty clinics, producing highly qualified specialists interested in ever-narrowing areas of practice. Until recently many of our medical schools remain ivory towers surrounded by disease-producing slums.

At least three nation-wide studies have been published in the past few years calling for the training of a "primary," "personal," or "family" physician. This physician in the words of the Ad Hoc Committee on Education for Family Practice of the American Medical Association's Council on Medical Education is one who:

"1. Serves as the physician of first contact with the patient and provides a means of entry into the health care system.

2. Evaluates the patient's total health needs, provides personal medical care in one or more fields of medicine, and refers the patient when indicated to appropriate sources of care while preserving the continuity of his care.

3. Assumes responsibility for the patient's comprehensive and continuous health care and acts as a leader or coordinator of the team that provides health services.

4. Accepts responsibility for the patient's total health care within the context of his environment, including the community and the family or comparable social unit.

The family physician himself would provide a high percentage of the medical services needed by his patients."

When the University of Arizona College of Medicine was planned, careful thought was given as to how this new school could best embark on a program most relevant to the medical needs of the state and nation. Among other things, we felt the appropriate context in which to educate the new breed of doctor would be in a setting where patients first enter the medical care system; where preventive medicine may be practiced at its optimum; where the physician practices as a primary, family doctor; where he may also learn how to best work with and utilize the skills of, the nurse, social worker, technologist and other aides.

Our plan is to develop a teaching resource in a community in Tucson which will supplement the basic science and university hospital and clinical facilities. The community we have selected is a fortunate choice in that it is one of great medical need – high morbidity and mortality rates – and deficient in resources for meeting these needs. It is a poverty area with the adverse environmental hazards that accompany poverty. It is also in the area which the city of Tucson plans to rehabilitate via the Model Cities Program. The area offers a unique opportunity for a merger of health care and environmental measures to improve the health status of this population.

A word about the population in the area: There are some 22,000 people living in the Model Cities area. We propose to focus our health effort on a target population of 10,000 of these. One-third of the 22,000 live in "extreme poverty" i.e., they are either on public assistance or have annual family incomes below $3,000.00. Forty-eight per cent of the total population have family incomes below $3,600.00. Ethnically, seventy-four per cent are Mexican-American and fourteen per cent are non-white. Almost fifty per cent of the housing is substandard. For example, 400 homes have outside privies.

The infant mortality rate is fifty per cent higher, prematurity rate one-third higher, the birth rate one-third higher and the rate of illegitimate births twice that of the remainder of Tucson.

The physician to population ratio is only one-half that of Tucson as a whole. The percentage of specialists is significantly less than that of Tucson as a whole, and the average age of the physicians in the area is four years greater than that of the physicians in Tucson as a whole.

Although the model neighborhood population makes up only seven per cent of the city's population, it accounts for twenty-five per cent of the admissions to the Pima County Hospital. The recent study of Steinle Associates of health resources in Tucson called attention to the great need for improved ambulatory and emergency services in southwest Tucson in which the model neighborhood is located.

Of the target population which we plan to serve, at least one-third are now receiving their medical care from County Hospital. The county hospital is over-burdened and it is hoped that the neighborhood health center will relieve some of the county hospital's outpatient burden.

The neighborhood health center program aims to provide medical care which is comprehensive, and will be concerned with continuity, high quality and personal concern for the patient. Specifically, we will provide comprehensive primary care in the outpatient facility, home care and in-hospital care. There will be twenty-four hour service. The health center itself will be open twelve hours each weekday, nine hours on Saturday and will have twenty-four hour telephone service; and an automobile and drivers for the transportation of those patients who have no other means. The staff will consist primarily of generalists: i.e., general practitioners, pediatricians and internists backed up by the necessary specialists and paramedical support. Physicians will be full and part-time on salary with appointments to the Department of Community Medicine and where appropriate, other departments of the College of Medicine. Already a number of local physicians have indicated interest in working at the health center. The neighborhood health center will closely coordinate its efforts with that of the Pima County Health Department, the Tucson-Southern Counties Mental Health Program and other health agencies.

There will be a special program devised to hire and train many persons from the community. These will be mainly people with very limited education and no skills and they will be trained as family health workers and technologists of various types. The family health worker will assist the public health nurse in home visiting, working in the clinic and participating in many of the other functions of the health center. It is hoped that these unskilled people will become skilled and will be able to move upward in social station as they improve their skills.

The residents of the neighborhood will participate in the affairs of the health center on an advisory level. They will constitute our feedback, our main instrument in the promulgation of good health practices in the community, etc.

The neighborhood health center will utilize the county hospital, the university hospital when it is completed and various other voluntary hospitals. We hope to assist in improving the family practice residency of the Tucson Hospital Medical Education Program. There will be a program of research and evaluation of all aspects of the neighborhood health center's activities including new uses of personnel, the impact of the program on the health status of the community, the utilization of the program by the community, and costs of medical care. Hospitalization should be reduced by the provision of comprehensive ambulatory care.

Medical students will learn about medicine under supervision at the health center. They will start in their first year, taking on a variety of responsibilities starting with observation and progressing to patient care. Each student will have responsibility for a specific number of families. The students will participate in the activities of the center on all levels including meetings and group work with the physicians, nurses, social workers, family health workers, etc. The impact on the medical student will also be studied and it will be interesting to see whether this experience will influence attitudes and career choices of the students.

Above and beyond our primary educational objective in developing the health center, we will be helping to bring good health care to a segment of the Tucson population which is seriously deficient in health care resources. In this time of poverty and unrest in our cities, we have an opportunity here for the College of Medicine and the practicing medical profession to collaborate in a project which could be an example worthy of emulation in other cities. We hope, too, that the neighborhood health center will prove to be an important resource to the practicing medical community. We will open the doors of the health center to the surrounding medical community for participation in our work, in our conferences and for refresher courses in continuing education. We invite your wholehearted participation in helping us to develop this program.

Although this discussion has dwelt largely with plans for the neighborhood health center, it would not be complete without mentioning our teaching program in epidemiology, environmental medicine and public health. Moreover, as a state institution our resources are available to the entire state. We would very much like to assist medical societies, voluntary and official health organizations, and other community groups in the various community health problems with which they may be faced.

NEW R.V.S. COMING

A new edition of the *Relative Value Studies* will be published by the California Medical Association in September.

The *Relative Value Studies,* or "*RVS,*" is a complete listing of procedures performed by physicians. There are also unit values which indicate the relationship of values of services to each other.

The *RVS* will become effective for usage in California April 1, 1970. It is designed to assist doctors, health insurance carriers, consumers and business to identify procedures which physicians perform. Furthermore, the edition serves as a guide to understanding the basis for charges. However, this is not a fee schedule.

The first edition of the *RVS* was published in 1956. Its concept has been adopted by other state medical societies and applied to voluntary health insurance and government-financed programs nationwide.

Revised by the California Medical Association's Committee on *RVS,* the 1969 edition is the culmination of more than two years of intensive study and consultation with experts in the health care profession.

"The content of this edition (of the *RVS*) reflects as completely as possible the manner in which medicine is practiced in California at this time," William H. Thompson, M.D., Chairman of the CMA Committee on *RVS*, said.

Major changes are: (1) expansion of the coding system from four to five digits; (2) inclusion of approximately 50 per cent more procedures than in the 1964 edition; (3) introduction of the concept of "modifiers"; (4) structuring of each RVS section unit values in such a way as to make them applicable to only that individual section; and (5) reorganization of the musculoskeletal system in the Surgery Section entirely according to body system.

A system of two-digit "modifier" codes for physicians was introduced so they may easily indicate circumstances which may affect the fee charged — either up or down — for a specific procedure.

There are a number of changes in specific sections. For example, in the medicine section, physician visits have been further refined to describe more accurately their relative complexity. New subsections have been added to describe services provided in extended care facilities and in hospital emergency rooms. Also included are many diagnostic services which were formerly included in "Surgery" (such as procedures relating to the eye, ear and the cardiovascular system).

Another major revision is the listing of all vascular injections for radiology in the "Surgery" section only, with cross-reference appearing in "Radiology." The "Laboratory" section, now called "Pathology," was reorganized according to the type of procedure performed rather than by the source of the specimen.

More than 20 medical specialty subcommittees and a number of individual consultants — comprising nearly 100 physicians — and representatives of the insurance industry, component medical societies and computerized billing services were consulted "in an attempt to make this edition as useful as possible," Dr. Thompson explained.

The format of the book has been improved with an edge index to make it easier to find and turn to particular sections. The subject index will be more detailed in its listing of procedures.

Copies of the revised *RVS*, at $3.50 each (including tax), will be available from Six-Ninety-Three Sutter Publications, Inc., 693 Sutter Street, San Francisco 94102. Prepaid orders will be filled beginning October 1.

TEN RULES FOR AVOIDING LAWSUITS

A Cleveland attorney has suggested ten rules to help doctors avoid appearing in court as defendants. In the February, 1969, issue of *The Physician's Legal Brief*, R. Crawford Morris, who specializes in defending medical liabilities cases, suggested the following rules:

(1) The physician usually can decline to accept a patient. However, Mr. Morris cautions the physician, that while he has an option to step aside, he must do so before he places himself in a position of abondoning the patient.

(2) Never guarantee a cure. The physician who promises a cure or uses language intimating such promise can be sued, not only for negligence, but for breach of contract as well, if the promised results do not materialize.

(3) Watch the time factor, especially if there has been an unfortunate result. This rule relates to the statute of limitations as they vary in each state.

(4) Keep up with the advances in medicine. A physician will be judged by what is considered good medical care at the time he renders treatment.

(5) Do not use unnecessary experimental procedures. Mr. Morris advises that if a physician finds such procedures necessary, he should announce it frankly as such and obtain a written informed consent for the procedure.

(6) Make a simple, reasonable disclosure of the risks involved, unless there is a therapeutic reason for not telling the patient. In these instances it is advisable to tell the patient's relatives, but obtain an informed consent from the patient for everything done.

(7) Keep good records. Should a trial ensue, records are important because they always are admissible as evidence, while witnesses to an event may not be available.

(8) Cooperate with the medical profession. This rule is laid down in an effort to caution physicians against loose talk which can promote law suits.

(9) Do not be hesitant about consultation. Mr. Morris cited a case he tried and won because there were numerous consultations in an effort to make a correct diagnosis. The diagnosis was incorrect, but the best men in town were called in for consultations which refuted a claim that the physician's conduct was negligent.

(10) Maintain good public relations. Mr. Morris noted that a physician should "be as careful with your tongue as you are with your scalpel." Incidents, in which patients overhear comments about their condition, can constitute inferior medical practice, as well as poor public relations, and are apt to promote law suits.

AM Medical History

WALTER REED, M.D.

Audrey Davis Stevens

WALTER REED IN 1876

From a photograph taken in Harrisonburg, Va. Ætat 25

This year, the Walter Reed Memorial Hospital probably has been mentioned in the news more often than most hospitals. A review has been made of some of Dr. Reed's great accomplishments in medicine but little, if any, mention has been made that Dr. Reed spent four years as a physician for the United States Cavalry in Arizona. He did not make any huge contributions to the medical world at that time but, nevertheless, his life in Arizona was an eventful and a happy one.

A few weeks prior to his journey to Arizona he married Emily Lawrence. Due to Arizona's hot summers, it was decided that Mrs. Reed should follow the Doctor in the fall when the weather was cooler. Because of this decision, the young 25-year old doctor and his 20-year old bride had but a few weeks together before he left in May (1876) for one of the hottest of all army posts.

Five months later, however, Mrs. Reed's journey was not what one would describe, even in those days, as a comfortable one. She experienced a train collision, a blizzard in Wyoming, and a stormy passage on a steamer from San Francisco to San Diego where she was met by her groom. Together, with a driver, they rode a doherty wagon, a "grandpappy" of the stagecoach, stopping at various stations along the route for a night's rest. This uncomfortable journey from San Diego to Fort Lowell lasted for almost three weeks.[1]

To put it mildly, Fort Lowell was quite a shock for the former Southern belle. Tucson, the closest to civilization that Mrs. Reed was to see for several years, consisted of a few general stores, wagon shops, and several saloons that specialized in liquor and the type of women who enjoyed the affections of quite a turnover of men. Needless to say, friends of the Reed's were mostly Army personnel! They confined their entertainment to picnics, teas and sewing circles.

After a year at Fort Lowell, Dr. Reed was transferred to Fort Apache and like the journey from San Diego to Fort Lowell, the trip was a dangerous one. Actually it was a suspense-packed ten days' journey. For example, one day the Reed party kept their weapons ready to fire at anything resembling an Indian. The reason for this precaution was that this particular section of Arizona Territory was reputedly inhabited by outlaw Indians. As a matter of fact, a week before their trip, a stage coach driver was killed by the Indians.

In spite of their worries, they arrived in Fort Apache complete with all their baggage, their dog and happy plans for their future. Mrs. Reed became acquainted with the Indians who lived at the post and became less fearful of this race of people.

While practicing medicine among the army personnel, ranchers and the friendly Indians, Dr. Reed's interest in yellow fever started to germinate. He also enjoyed going hunting with members of the Post and a few friendly Indians. On one of these hunting sprees, the group returned to Fort Apache with 41 deer and 50 turkeys. This cache was sufficient to supply everyone at the Post with a fine Christmas dinner (1879).

By the time they left Arizona Territory, their son, Walter Lawrence Reed, was a healthy two-year old. They were also guardians of a young Indian girl who had been found in a deserted Indian Camp by the Fort Apache cavalry and left as dead.

At a time when an Indian was considered, by most westerners, a savage and only "a dead Indian was considered a good Indian," the Reeds took the little girl into their home and named her Susie. She lived with them approximately twelve years and then lived with the Indians at Mount Vernon Barracks where she taught them the English language. Later, she moved with the tribe to Fort Sill, Oklahoma. She died there about 1902. By coincidence, this was the same year Dr. Walter Reed died from a ruptured appendix.

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In Memoriam

VAN A. SMELKER, M.D.

1883-1969

Dr. Van A. Smelker, one of the last of the truly pioneer physicians of the great Southwest, passed away in Tucson on June 26, 1969. He was 86 years old and had continued to practice until two months before his death, a span of 64 years.

He received his M.D. degree at Northwestern University Medical School in 1905. He practiced in Chicago until he went to Sinaloa, Mexico, in 1908 as physician for Sud Pacifico de Mexico Railroad. He obtained a license to practice in Arizona and moved to Nogales in 1909 where he lived until he came to Tucson in 1932. He became proficient in reading and writing the Spanish language and built a considerable practice with patients from the interior of Mexico. I knew Dr. Van Smelker from the time he came to Tucson in 1932. He was a retiring, kindly man who placed service to his fellow man far above personal gain or fame. He was meticulous in his care of the sick. He exemplified the highest traditions of the medical profession.

The following editorial published in the Arizona Daily Star is a fitting tribute to this pioneer Arizona physician.

> "The death last week of 86-year-old Dr. V. A. Smelker brought to a close one of the most remarkable medical careers in the great Southwest.
>
> "Dr. Smelker practiced in Arizona for 61 years. His patients stretched from Central Arizona deep into Sonora, Mexico, and his friends stretched from coast-to-coast and border-to-border. A 1905 graduate of Northwestern University Medical School, the venerable physician obtained his Arizona license in 1908, following which he went to Sinaloa, Mexico as an assistant physician for the Southern Pacific Railroad. Returning to Arizona in 1909, he practiced in Nogales until 1932 and then moved to Tucson where he remained active until two months ago.
>
> "Dr. Smelker did much to cement relations between the United States and Mexico, because many of his patients, including former Presidents Obregon, Calles and Rodriguez, were from Mexico. He also ministered to the wounded on both sides during the Pancho Villa revolution in Mexico.
>
> "He will be well remembered as a 20th century medical pioneer with deep roots in two nations."

Letters to Editor

Robert F. Lorenzen, M.D., Editor
Arizona Medicine

Dear Doctor Lorenzen:

Doctor Flynn is to be congratulated on his "President's Page" on periodic relicensure. The Arizona Medical Association deserves tremendous credit for passing Resolution No. 10 on periodic medical relicensure.

Doctor Flynn has expressed himself so eloquently and wittily that little remains to be said. Let me add, however, that after sitting on the Board of Medical Examiners for more than four years I can vouch for the need to investigate this problem thoroughly and to do something about it.

Arizona has already made a wonderful beginning. In our recent statute covering medical licensure we have established the need to reexamine candidates who wish to practice in Arizona by means of reciprocity endorsement. The time limit in these instances is fifteen years. In other words, anyone who has obtained his license more than fifteen years ago must undergo an oral examination.

I have always wondered why we in Arizona consider ourselves immune to the inroads of old age, sickness, creeping ignorance, etc. We feel that anyone who has not practiced in the state during these last fifteen years should be examined but those of us who have been fortunate enough to be exposed to Arizona's eternal sun are supposedly free from all these risks.

This principle, however, does not apply to our driver's license. Here the state has ordained that we shall be reexamined every three years, and rightly so.

It is about time that we adopt these principles in our laws. We must be able to assure our public that licensed physicians not only were knowledgeable, skillful and worthy to practice medicine some fifteen, thirty or fifty years ago, but they have remained capable through all these years. How could we do it except by periodic relicensure?

It will take a lot of consideration to determine the best method of periodic reevaluation of a physician's capacities.

Arizona is for once in the lead, at least as far as relicensure for reciprocity candidates is concerned. Let us extend this same principle to the rest of the practicing physicians in this state and hopefully in the nation.

By the way, while we are thinking along these lines, how about investigating the possibility of licensing people only in the area of their own competence? I as a psychiatrist am theoretically permitted, under my state license to practice both medicine and surgery, to perform eye surgery, thoracic surgery, cardiac surgery, etc. etc. without a day's training or experience. Is this right? Should not the state protect is citizens from unscrupulous practitioners who overstep their competence?

Sincerely yours,
Otto L. Bendheim, M.D.

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6TH NATIONAL CANCER CONFERENCE – NOTES

September 1968, Denver

Present status and future prospects of organ transplantation in cancer surgery. There is evidence that this form of treatment will not be helpful. The suppression of the host immunilogical mechanism with the use of Imuran, a cortico-steroid, and anti-lymphocytic globulin renders the host more susceptible to infection and to the development of tumors. Experience has shown that the patients receiving organ transplants have an increased number of cancers developing primarily in the host or in the donated organ which were not previously evident.

Thomas E. Starzl, M.D., Professor of
Surgery, University of Colorado
Medical Center, Denver

Dr. William L. Donegan of the Ellis Fischel State Cancer Hospital in discussing management of the primary and operable breast carcinoma showed that their results are identical whether they use:

1. The standard radical mastectomy.
2. The extended radical mastectomy as advocated by Dr. Urban.
3. The modified radical as advocated by Dr. Sugarbaker.

. . . .

The Role of Super-radical Operations for Breast Cancer.

The internal mammary node is invaded early and frequently. Three quarters of the lymph drainage of the breast is to the axilla, however in inner and central quadrant lesions 60% of the patients with breast cancer have internal mammary lymph node involvement; of this group 15% have negative axillas. He finds carcinoma in the opposite breast in 9% of the patients. One third of the patients receive 4500 Roentgen to the supraclavicular area on the involved side.

Jerome A. Urban, M.D., Clinical Assistant
Professor of Surgery, Cornell University,
Associate Attending Surgeon Memorial
Hospital, New York, New York

If she asks what you think of babyScott

The next page will help you answer.

Introducing the babyScott diaper system. Designed with infants, mothers, and physicians in mind.

Two-part system offers clinical advantages as well as convenience and efficiency.

The diaper panty: it takes anatomy into consideration. The babyScott diaper panty is specifically designed to hold the babyScott disposable diaper securely, yet without constriction. The panty fits low in front to avoid pressure on the umbilicus. And high on the legs so it won't chafe, bind or interfere with mobility.

Four different sizes and multi-position snaps help assure good fit and comfort. "Safety" pins, which can always pose a threat, are completely unnecessary.

All portions of the panty that come in contact with the infant's skin are covered with soft, quick-drying cloth.

Essentially non-absorbent, the babyScott panty can be thoroughly and rapidly washed, rinsed and dried.

The disposable diaper: it takes sensitive skin into consideration. The disposable diaper, itself, is thick, fluffy and soft. Its layers of highly absorbent cellulose fluff are covered by a web-like liner, which is both permeable and relatively hydrophilic to help keep infants drier.

Doubly thick for extra absorption in front, the diaper fans out bucket-seat fashion in the back for wide coverage. The babyScott diaper thus provides excellent protection while minimizing bunching and consequent irritation. On those occasions when double diapers are used for extra protection comfort is still maintained

With babyScott, each diaper comes fresh and clean out of the pack. It's used only once, then flushed away or otherwis disposed of.

No soap, detergent or bleach residues. No opportunity for cross contamination from the diaper.

A frequently changed infant is a healthier, happier infant.
And the babyScott diaper system is so easy to use, it will be used.

babyScott®
the pinless diaper

Another fine quality product from Scott Paper Company

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The SEMINAR is designed to acquaint physicians, nurses and other health sciences practitioners with the capabilities of MEDLARS, the National Library of Medicine's computer-based medical literature retrieval system.

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the "daytime sedative" for everyday situational stress

When stress is situational—environmental pressure, worry over illness—the treatment often calls for an anxiety-allaying agent which has a prompt and predictable calming action and is remarkably well tolerated. Butisol Sodium (sodium butabarbital) meets this therapeutic need.

After 30 years of clinical use . . . still a first choice among many physicians for dependability, safety and economy in mild to moderate anxiety.

Contraindications: Porphyria or sensitivity to barbiturates.

Precautions: Exercise caution in moderate to severe hepatic disease. Elderly or debilitated patients may react with marked excitement or depression.

Adverse Reactions: Drowsiness at daytime sedative dose levels, skin rashes, "hangover" and systemic disturbances are seldom seen.

Warning: May be habit forming.

Usual Adult Dosage: As a daytime sedative, 15 mg. (¼ gr.) to 30 mg. (½ gr.) t.i.d. or q.i.d.

Available for daytime sedation: Tablets, 15 mg. (¼ gr.), 30 mg. (½ gr.); Elixir, 30 mg. per 5 cc. (alcohol 7%).
BUTICAPS® [Capsules Butisol Sodium (sodium butabarbital)] 15 mg. (¼ gr.), 30 mg. (½ gr.).

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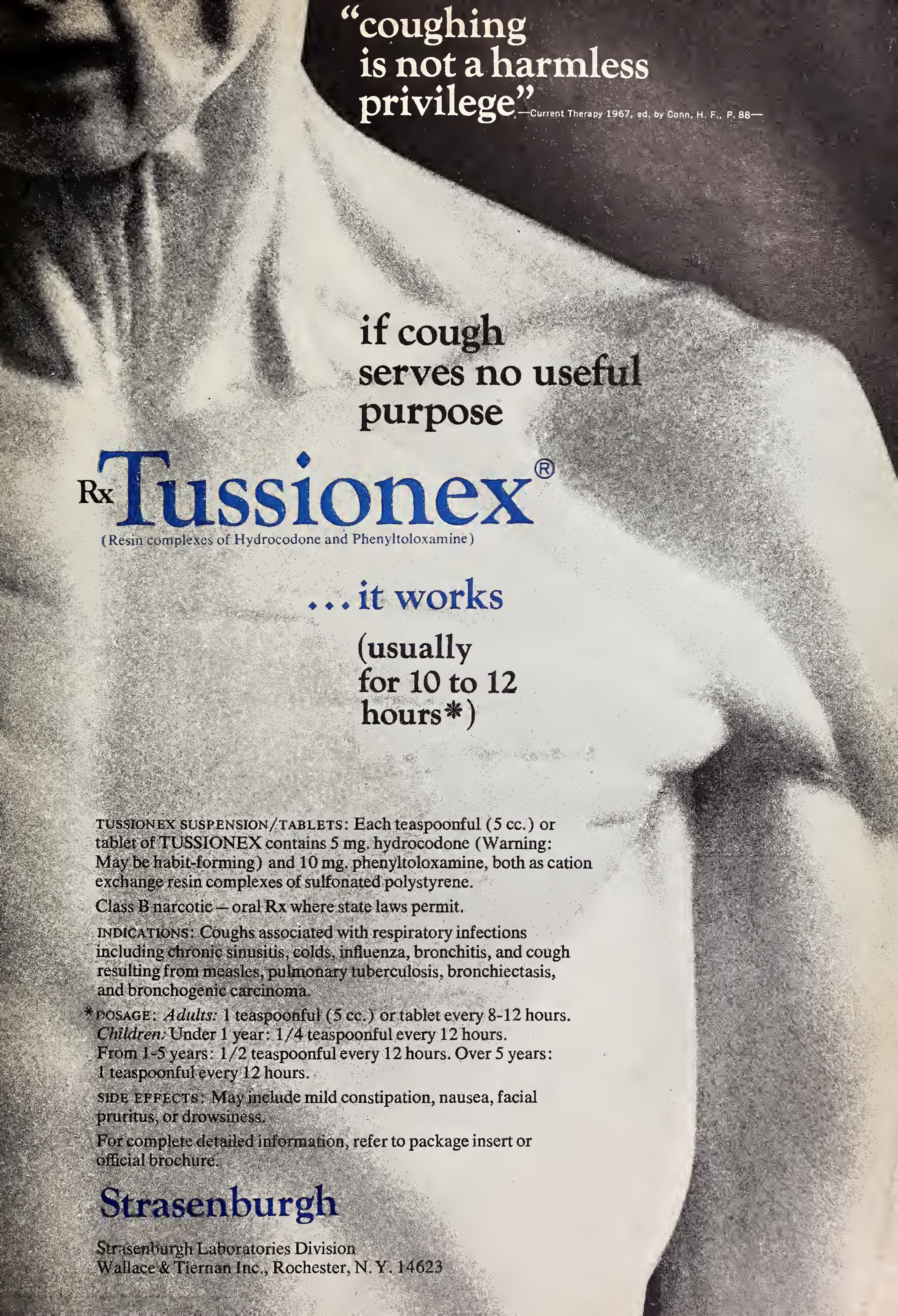
McNeil Laboratories, Inc., Fort Washington, Pa.



"coughing
is not a harmless
privilege"—Current Therapy 1967, ed. by Conn, H. F., P. 88—

if cough
serves no useful
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Rx **Tussionex**®
(Resin complexes of Hydrocodone and Phenyltoloxamine)

...it works
(usually
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TUSSIONEX SUSPENSION/TABLETS: Each teaspoonful (5 cc.) or tablet of TUSSIONEX contains 5 mg. hydrocodone (Warning: May be habit-forming) and 10 mg. phenyltoloxamine, both as cation exchange resin complexes of sulfonated polystyrene.

Class B narcotic—oral Rx where state laws permit.

INDICATIONS: Coughs associated with respiratory infections including chronic sinusitis, colds, influenza, bronchitis, and cough resulting from measles, pulmonary tuberculosis, bronchiectasis, and bronchogenic carcinoma.

*DOSAGE: *Adults:* 1 teaspoonful (5 cc.) or tablet every 8-12 hours. *Children:* Under 1 year: 1/4 teaspoonful every 12 hours. From 1-5 years: 1/2 teaspoonful every 12 hours. Over 5 years: 1 teaspoonful every 12 hours.

SIDE EFFECTS: May include mild constipation, nausea, facial pruritus, or drowsiness.

For complete detailed information, refer to package insert or official brochure.

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Strasenburgh Laboratories Division
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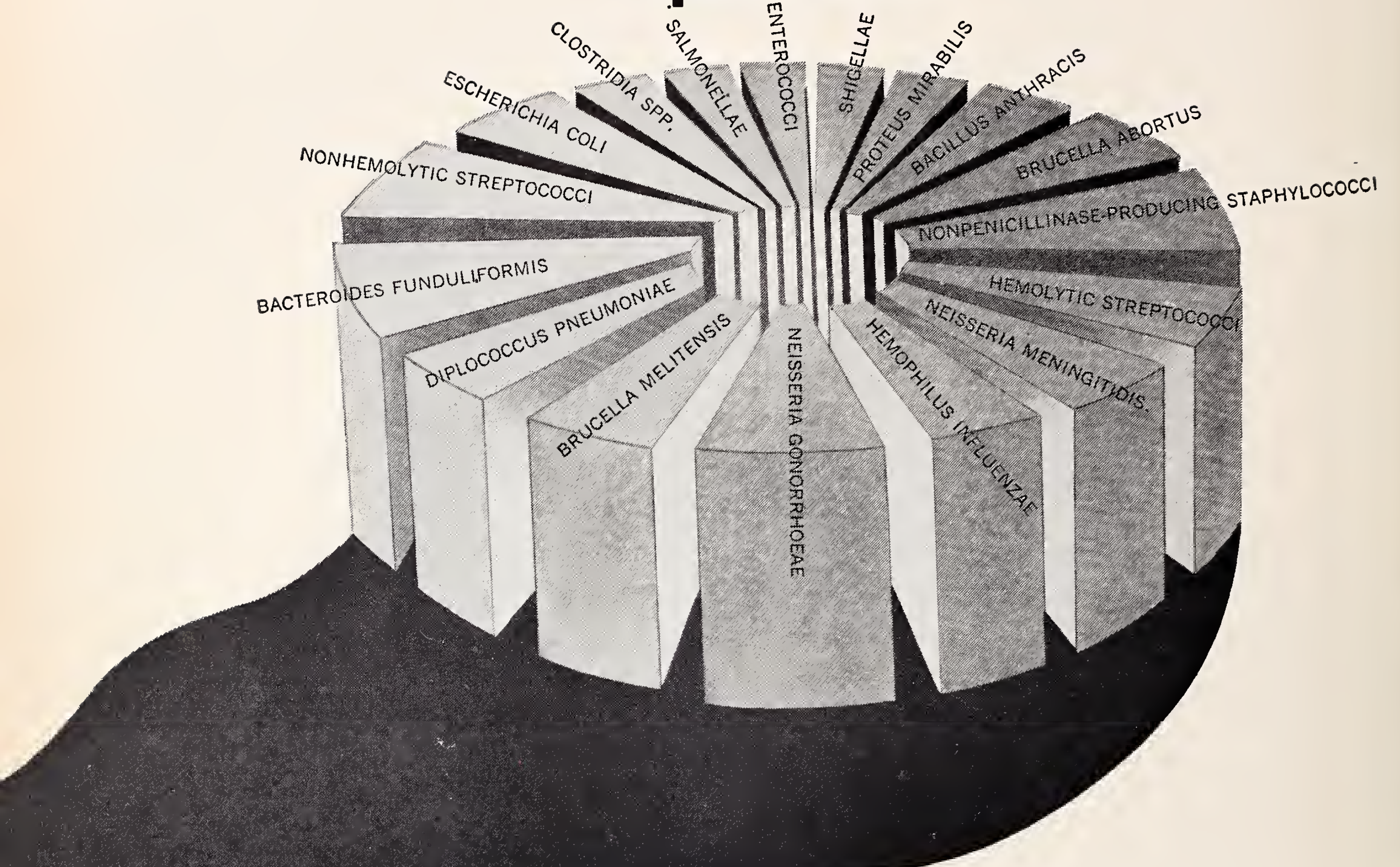
With the broad Polycillin (ampicillin trihydrate) spectrum...



...you have a lot going for you in the wide range of bacterial infections.

PRESCRIBING INFORMATION. For complete information consult Official Package Circular. **Indications:** Infections due to susceptible strains of Gram-negative bacteria (including Shigellae, *S. typhosa* and other Salmonellae, *E. coli, H. influenzae, P. mirabilis, N. gonorrhoeae* and *N. meningitidis*) and Gram-positive bacteria (including streptococci, pneumococci and nonpenicillinase-producing staphylococci). **Contraindications:** A history of allergic reactions to penicillins or cephalosporins and infections due to penicillinase-producing organisms. **Precautions.** Typical penicillin-allergic reactions may occur, especially in hypersensitive patients. Mycotic or bacterial superinfections may occur. Experience in newborn and premature infants is limited and caution should be used in treatment, with frequent organ function evaluations. Safety for use in pregnancy is not established. In gonorrheal therapy, serologic tests for syphilis should be performed initially and monthly for 4 months. Assess renal, hepatic and hematopoietic function intermittently during long-term therapy. **Adverse Reactions:** Skin rash, pruritus, urticaria, nausea, vomiting, diarrhea and anaphylactic reactions. Mild transient elevations of SGOT or SGPT have been noted. Black tongue has been noted in some patients receiving the Chewable Tablets. **Usual Dosage:** Adults—250 or 500 mg. q. 6 h. (according to infection site and offending organisms). Children—50-100 mg./Kg./day in 3 to 4 divided doses (depending on infection site and offending organisms). Bacterial meningitis—150-200 mg./Kg./day in 6 to 8 divided doses. Children weighing more than 20 Kg. should be given an adult dose when prescribing orally. In parenteral administration, children weighing more than 40 Kg. should be given an adult dose. Beta-hemolytic streptococcal infections should be treated for at least 10 days. **Supplied:** Capsules—250 mg. in bottles of 24 and 100. 500 mg. in bottles of 16 and 100. For Oral Suspension—125 mg./5 ml. in 60, 80 and 150 ml. bottles. 250 mg./5 ml. in 80 and 150 ml. bottles. Chewable Tablets—125 mg. in bottles of 40. Injectable—for I.M./I.V. use—vials of 125 mg., 250 mg., 500 mg., and 1 Gm. Pediatric Drops—100 mg./ml. in 20 ml. bottles.

11-1/2/69 **A.H.F.S. Category 8:12.16**

Polycillin®
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The penicillin you use like a broad-spectrum antibiotic

Dulcolax®...so predictable you can almost set patients by it.

Dulcolax works so effectively that the time of bowel evacuation can often be predicted.

Dulcolax tablets taken at night will usually result in a convenient bowel movement the following morning. Dulcolax suppositories generally work within 15 minutes to an hour.

Dulcolax may be given to the aged, pregnant or nursing women, and children. It may be particularly helpful in conditions in which straining should be avoided. The drug, however, is contraindicated in the acute surgical abdomen.

Dulcolax® bisacodyl

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The casual atmosphere of Camelback Hospital
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Looking east, Camelback Mountain provides the background
for the lovely lawn and grove area.
The natural beauty of the surroundings at Camelback Hospital
creates, for the patient,
a restful, scenic setting.

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Located in the heart of the beautiful Phoenix citrus area near picturesque Camelback Mountain, the hospital is dedicated exclusively to the treatment of psychiatric and psychosomatic disorders, including alcoholism.

APPROVED BY THE JOINT COMMISSION ON ACCREDITATION OF HOSPITALS; and THE AMERICAN PSYCHIATRIC ASSOCIATIO

The AMBAR® SCRAPBOOK of
Obesity Oddities
FACT & LEGEND
OBESITY WAS A MILITARY OFFENSE!
OVERWEIGHT ROMAN HORSEMEN WERE MADE TO FORFEIT THEIR MOUNTS AND BECOME FOOT SOLDIERS!
RECORDED ON AN ENGLISHMAN'S TOMBSTONE
JAMES PARSON
DIED 1743
HE HAD OFTEN EATEN A WHOLE SHOULDER OF MUTTON AND A PECK OF HASTY PUDDING
SHAKESPEARE WAS AWARE OF THE DANGERS OF OBESITY HE WROTE...
Make less thy body hence and more thy grace, leave gormandizing; Know thy grave doth gape for thee wider than for other men.
100
Ambar No.2 Extentabs
Rx
THE COST OF AMBAR EXTENTABS IS APPROXIMATELY ONE HALF THAT OF OTHER LEADING APPETITE SUPPRESSANTS
AN IMPORTANT FACTOR IN LONG TERM THERAPY

CONTROL FOOD AND MOOD ALL DAY LONG WITH A SINGLE MORNING DOSE

AMBAR #2 EXTENTABS®

methamphetamine HCl 15 mg., phenobarbital 64.8 mg. (1 gr.) (Warning: may be habit forming).

One Ambar Extentab before breakfast can help control most patients' appetite for up to 12 hours. Methamphetamine, the appetite suppressant, gently elevates mood and helps overcome dieting frustrations. Phenobarbital, the sedative in Ambar, controls irritability and anxiety... helps maintain a state of mental calm and equanimity. Both work together to ease the tensions that erode the willpower during periods of dieting.

Also available: Ambar #1 Extentabs®—methamphetamine hydrochloride 10 mg., phenobarbital 64.8 mg. (1 gr.) (Warning: may be habit forming).

BRIEF SUMMARY/**Indications:** Ambar suppresses appetite and helps offset emotional reactions to dieting. **Contraindications:** Hypersensitivity to barbiturates or sympathomimetics; patients with advanced renal or hepatic disease. **Precautions:** Administer with caution in the presence of cardiovascular disease or hypertension. **Side Effects:** Nervousness or excitement occasionally noted, but usually infrequent at recommended dosages. Slight drowsiness has been reported rarely. See package insert for further details.

A. H. ROBINS COMPANY,
RICHMOND, VA. 23220

A-H-ROBINS

heavenly relief for unearthly cough

Benylin®
EXPECTORANT

Each fluidounce contains: 80 mg. Benadryl® (diphenhydramine hydrochloride, Parke-Davis); 12 grains ammonium chloride; 5 grains sodium citrate; 2 grains chloroform; 1/10 grain menthol; and 5% alcohol. An antitussive and expectorant for control of coughs due to colds or of allergic origin, BENYLIN EXPECTORANT is the leading cough preparation of its kind. BENYLIN EXPECTORANT tends to inhibit cough reflex... soothes irritated throat membranes. And its not-too-sweet, pleasant raspberry flavor makes BENYLIN EXPECTORANT easy to take. PRECAUTIONS: Persons who have become drowsy on this or other antihistamine-containing drugs, or whose tolerance is not known, should not drive vehicles or engage in other activities requiring keen response while using this preparation. Hypnotics, sedatives, or tranquilizers if used with BENYLIN EXPECTORANT should be prescribed with caution because of possible additive effect. Diphenhydramine has an atropine-like action which should be considered when prescribing BENYLIN EXPECTORANT. ADVERSE REACTIONS: Side reactions may affect the nervous, gastrointestinal, and cardiovascular systems. Drowsiness, dizziness, dryness of the mouth, nausea, nervousness, palpitation, and blurring of vision have been reported. Allergic reactions may occur. PACKAGING: Bottles of 4 oz., 16 oz., and 1 gal.

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Detroit, Michigan 48232

PARKE-DAVIS

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vacation in
a vial:
the spasm
reactors
in your practice
deserve

"the Donnatal® Effect"

	each tablet, capsule or 5 cc. of elixir (23% alcohol)	each Donnatal No. 2	each Extentab®
hyoscyamine sulfate	0.1037 mg.	0.1037 mg.	0.3111 mg.
atropine sulfate	0.0194 mg.	0.0194 mg.	0.0582 mg.
hyoscine hydrobromide	0.0065 mg.	0.0065 mg.	0.0195 mg.
phenobarbital	(¼ gr.) 16.2 mg.	(½ gr.) 32.4 mg.	(¾ gr.) 48.6 mg.
(Warning: may be habit forming)			

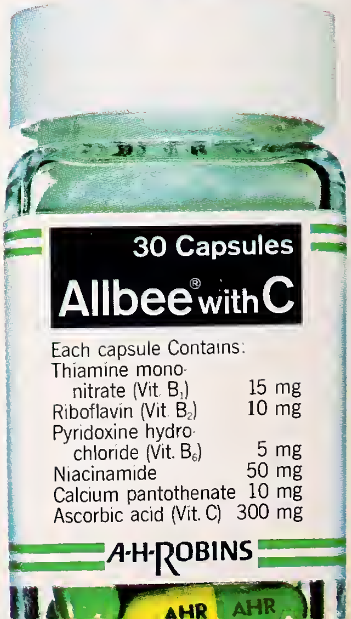
Brief Summary. Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Administer with caution to patients with incipient glaucoma or urinary bladder neck obstruction. Contraindicated in acute glaucoma, advanced renal or hepatic disease or a hypersensitivity to any of the ingredients.

A. H. ROBINS COMPANY, RICHMOND, VIRGINIA 23220

A·H·ROBINS

Two ways to provide your patients with a month's therapeutic supply of Vitamin C:

290 tangerines or 30 Allbee® with C.


30 Capsules
Allbee® with C
Each capsule Contains:
Thiamine mononitrate (Vit. B1) 15 mg
Riboflavin (Vit. B2) 10 mg
Pyridoxine hydrochloride (Vit. B6) 5 mg
Niacinamide 50 mg
Calcium pantothenate 10 mg
Ascorbic acid (Vit. C) 300 mg
A-H-ROBINS
AHR
AHR

Your patient would have to peel and eat 290 tangerines a month, almost 10 every day, to get as much Vitamin C as is contained in just one bottle of 30 Allbee with C capsules (taken one capsule daily). In addition, each capsule provides full therapeutic amounts of the B-complex vitamins. For example, as much niacin as 2 pounds of sirloin steak. This handy bottle of 30 Allbee with C capsules gives your patient a month's supply at a very reasonable cost. Also the economy size of 100. Available at pharmacies on your prescription or recommendation.

A. H. Robins Company, Richmond, Va. 23220

Because any
urologic infection
can be serious,
BREON introduces
potent therapy

for the strong start and a fast finish...

"...a significant gap appears to have been closed in the armory of drugs available to the urologist."[1]
Bacteriuria and symptoms can be eliminated within 48 to 72 hours; susceptible infection often in 10 to 14 days.

before your “minor” becomes a major problem

choice initial treatment for urinary infections

Cybis® (nalidixic acid) provides prompt broad gram-negative bactericidal activity at normal urinary pH range that can eradicate troublesome *E. coli,* Aerobacter and Proteus. A good starting drug, it can effectively accelerate management of infection due to sensitive organisms.

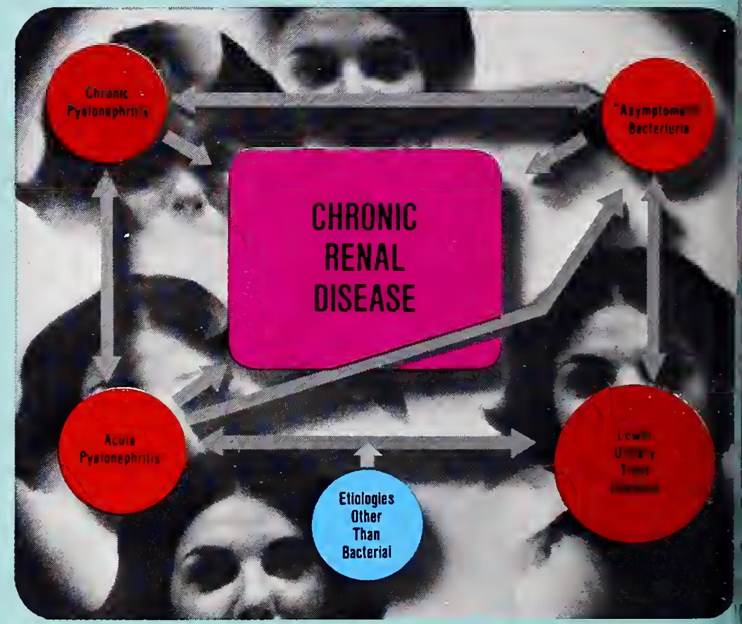
essential control within the primary 72-hour cycle

In cases of acute infection due to susceptible organisms, Cybis works well toward the rapid clearing of disease when obstruction is absent or can be relieved. Within 48 to 72 hours, symptoms are frequently eased and bacteriuria eliminated. Susceptible infection is often eradicated in 10 to 14 days.

blocks the young female progression of infection

Cybis can be useful in naturally susceptible young female patients with new or well-established urinary disturbances. Combining rapid potency with relative freedom of serious side reactions and toxicity, the drug can be of particular value in preventing higher tract involvement or blocking the possible continuum of disease. (See Chart)

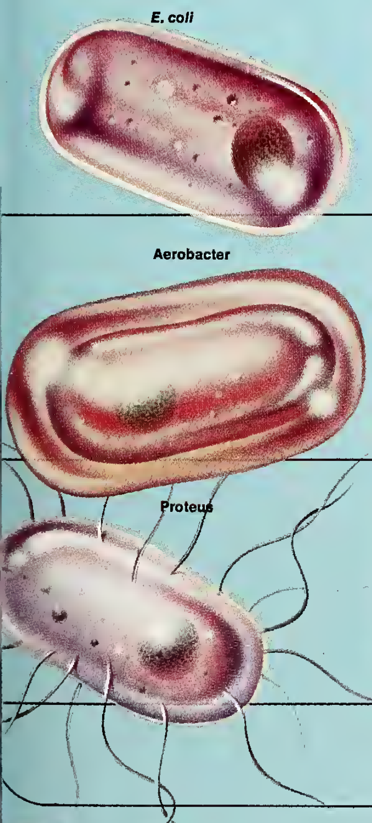
Kinetic Relationship of Acute and Chronic Bacterial Pyelonephritis to Chronic Renal Disease[2]



consistent activity against 706 gram-negative strains

In vitro testing of *E. coli,* Aerobacter and Proteus species showed better than 90% sensitivity to nalidixic acid.[3] (See Table)

etter Than 90% Sensitivity Among 3 Common Urinary Invaders



	Strains	Sensitivity to Nalidixic Acid	Sensitivity
E. coli	413	394	95%
Aerobacter	148	133	90%
Proteus	145	129	89%
	TOTAL 706	Average	91%

57 of 86 Pseudomonas species were resistant

References: 1. Reimann-Hunziker, R. and Reimann-Hunziker, G. J.: *Praxis 53*:15, Jan. 9, 1964. 2. Sanford, J. P.: *Med. Times 96*:715, July 1968. 3. Reese, L.: *Canad. M. A. J. 92*:394-397, Feb. 20, 1965.

Cybis®
(nalidixic acid)

or the strong start and a fast finish... in cystitis, pyelonephritis, prostatitis, urethritis

Before prescribing, please consult complete product information, a summary of which follows on the next page, including indications, warning, precautions, adverse reactions and dosage.

Summary of prescribing information

Indications: Urinary tract infections in which species of sensitive gram-negative bacteria are predominant, particularly *Proteus, Escherichia coli, Aerobacter, Klebsiella,* and certain strains of *Pseudomonas.* Gram-positive bacteria are less sensitive to Cybis but favorable clinical results have been observed.

Warning: Use in Pregnancy. This drug is not recommended in the first trimester of pregnancy. However, it has been used in several patients during the last two trimesters without producing apparent ill effects in either mother or fetus.

Precautions: Although prolonged treatment with Cybis has been generally well tolerated, as with all new drugs it is advisable to carry out blood, renal, and liver function tests periodically if treatment is continued for more than one or two weeks. The dosage recommended for adults and children should not be arbitrarily doubled unless under the careful supervision of a physician. **It should be used with caution in patients with liver disease, epilepsy, or severe cerebral arteriosclerosis, and in patients in whom kidney function is severely impaired.** Patients should be cautioned to avoid unnecessary exposure to direct sunlight while receiving Cybis and, if a photosensitivity reaction occurs, therapy should be discontinued.

During treatment microorganisms may develop resistance to this drug. Resistant bacteria, not previously present or identified, may emerge. Cultures should be taken and bacterial sensitivity tests made periodically, particularly if the clinical response is unsatisfactory or if a relapse occurs. Should resistance develop, other specific chemotherapy should be instituted; no cross resistance has been observed. If new strains of bacteria that are not sensitive emerge, other effective antibacterial agents may be added. When Benedict's or Fehling's solutions or Clinitest® Reagent Tablets are used to test the urine of patients taking Cybis, a false-positive reaction for glucose may be obtained due to the liberation of glucuronic acid from the metabolites excreted. However, a colorimetric test for glucose based on an enzyme reaction (using, for example, Clinistix® Reagent Strips or Tes-Tape®) does not give a false-positive reaction to Cybis glucuronide.

Adverse reactions: Mainly mild nausea, vomiting, and other gastrointestinal disturbances: less frequently, sleepiness, drowsiness, weakness, headache, dizziness and vertigo, and rarely cholestasis, paresthesia, thrombocytopenia, leukopenia, or hemolytic anemia which in some patients may have been associated with deficiency in activity of glucose-6-phosphate dehydrogenase. Itching, pruritus, rash, urticaria, mild eosinophilia, reversible photosensitivity reactions primarily involving exposed surfaces, and reversible subjective visual disturbances (overbrightness of lights, change in visual color perception, difficulty in focusing, decrease in visual acuity and double vision), occurred occasionally. Reversible increased intracranial pressure with bulging anterior fontanel, papilledema, and headache have been observed occasionally in infants and children. Toxic psychosis and brief convulsions (the latter generally in patients with possible predisposin factors, and both usually associated with excessive dosage) have been recorded in rare instances.

Dosage and administration: ***Adults*** **—Four Gm. da by mouth (2 tablets of 500 mg. four times daily) for o to two weeks. Thereafter, if prolonged treatment is indicated, the dosage may be reduced to two Gm. da (1 tablet of 500 mg. four times daily).** ***Children*** **— According to age and weight: approximately** ***25 mg. per pound*** **of body weight per day, administered in divided doses.**

Note: The dosage recommended above for adults a children should not arbitrarily be doubled unless un the careful supervision of a physician. Until further experience is gained, infants under 1 month should be treated with the drug.

How supplied: Tablets of 500 mg., bottles of 50.

Before prescribing, please refer to complete prescribing information.

Cybis®

(nalidixic acid)

for the strong start and a fast finish...

in cystitis
pyelonephritis
prostatitis
urethritis

1220
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500 mg.
brand of
nalidixic acid
(1-ethyl-1,4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3-carboxylic acid)
50 TABLETS
Caution: Federal law prohibits dispensing without prescription.
Usual adult dose: 500 mg. or 1 Gm. four times daily

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90 Park Avenue, New York, N.Y. 10016
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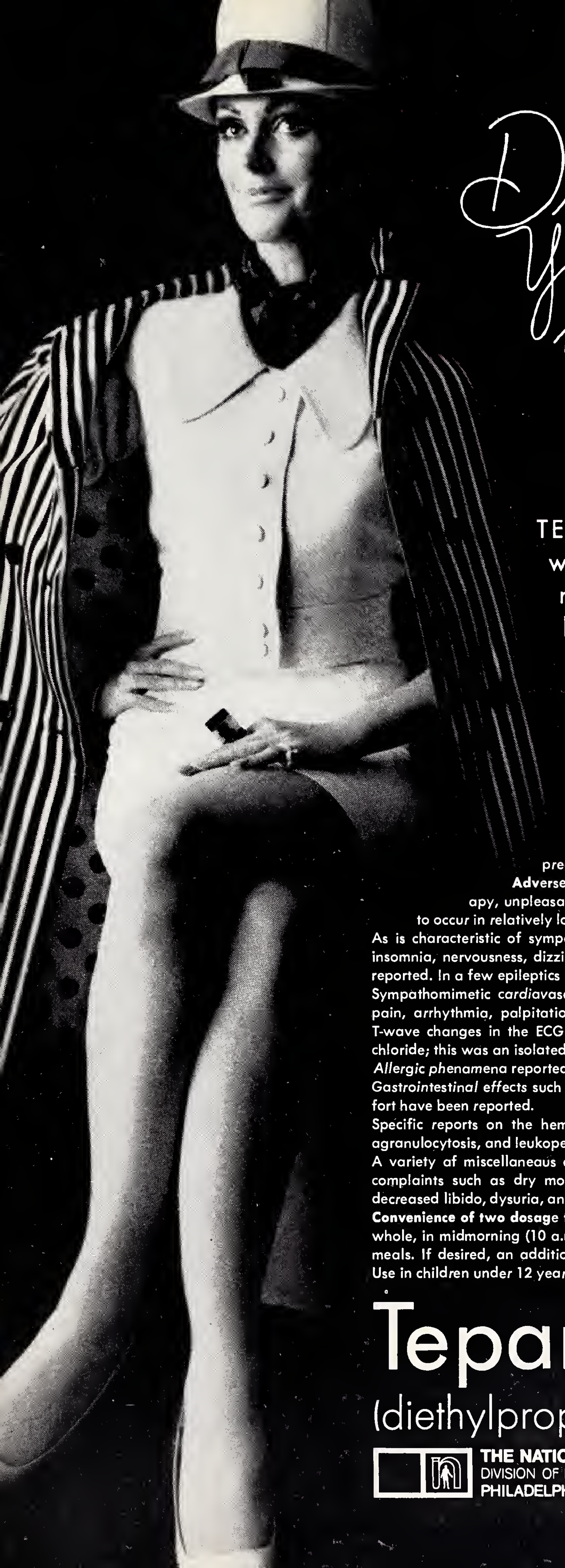


Dear Doctor,
You made me
what I am today -
a whole lot
slimmer!

TEPANIL—the right start in support of the weight-control program *you* recommend. It reduces the appetite. Doesn't kill it. Weight loss is significant—gradual—yet there is a relatively low incidence of CNS stimulation. Because TEPANIL works on the appetite, not on the "nerves."

Contraindications: Concurrently with MAO inhibitors, in patients hypersensitive to this drug; in emotionally unstable patients susceptible to drug abuse.

Warning: Although generally safer than the amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence.

As is characteristic of sympathomimetic agents, it may occasionally cause *CNS effects* such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptics an increase in convulsive episodes has been reported.

Sympathomimetic *cardiovascular effects* reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others.

Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema.

Gastrointestinal effects such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported.

Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia.

A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

Convenience of two dosage forms: TEPANIL Ten-tab tablets: One 75 mg. tablet daily, swallowed whole, in midmorning (10 a.m.); TEPANIL: One 25 mg. tablet three times daily, one hour before meals. If desired, an additional tablet may be given in midevening to overcome night hunger. Use in children under 12 years of age is not recommended.

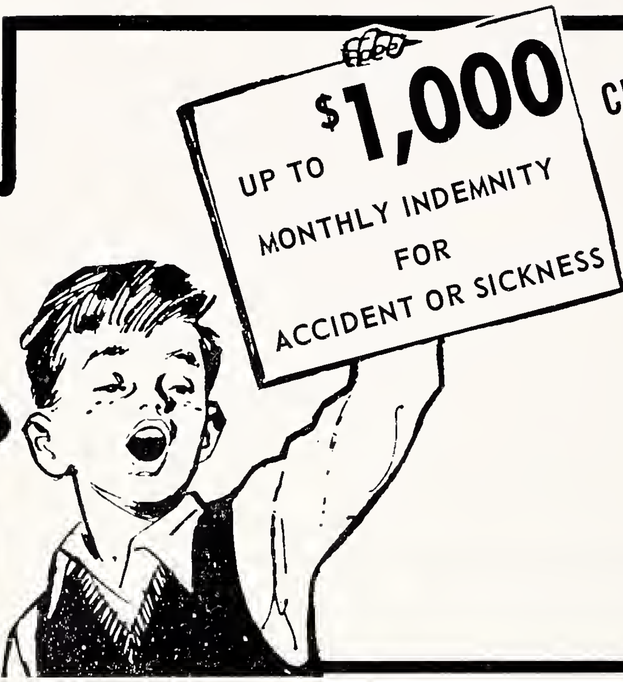
Tepanil® Ten-tab®

(continuous release form)

(diethylpropion hydrochloride)

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON-MERRELL INC.
PHILADELPHIA, PENNSYLVANIA 19144

T-918A U.S. PATENT NO. 3,001,910 5/69



UP TO $1,000
MONTHLY INDEMNITY
FOR
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MONTHLY INDEMNITY	$300	$1,000
AGE AT ENTRY AND ATTAINED AT RENEWAL	STD. 5 YR. ACC. 2 YR. SICK.	STD. 5 YR. ACC. 2 YR. SICK.
UNDER 35	44.50	132.00
35–39	48.70	136.20
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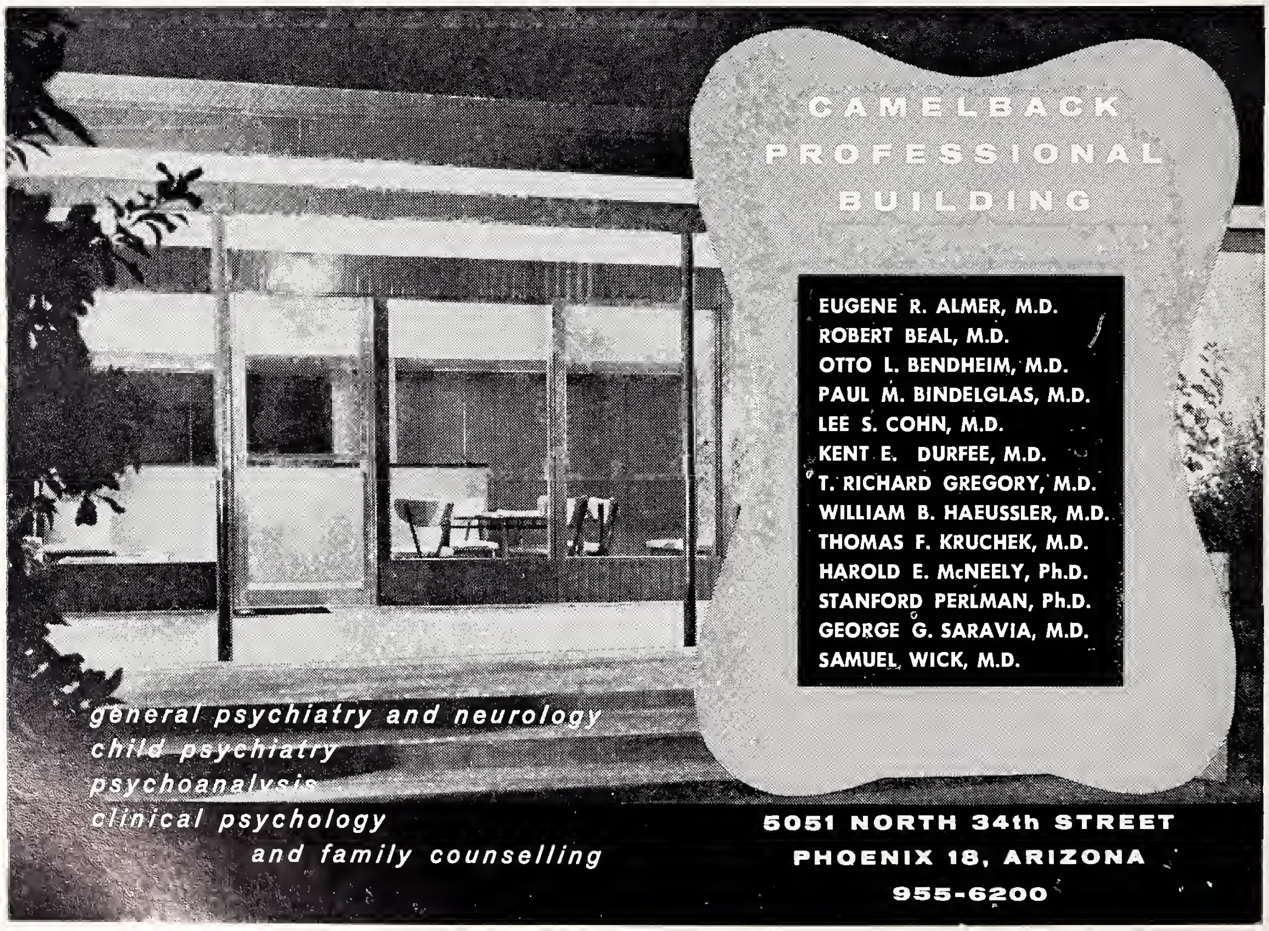

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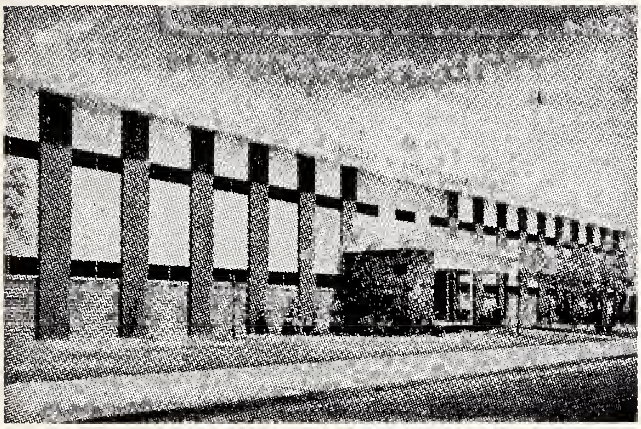

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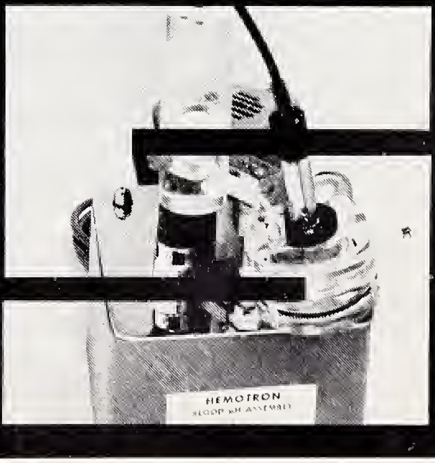

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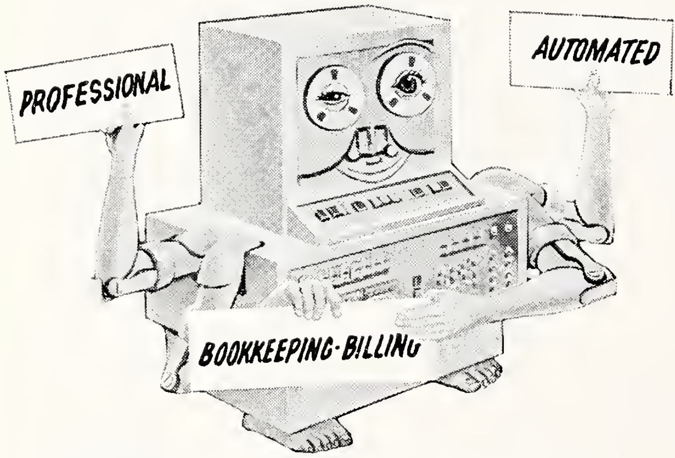

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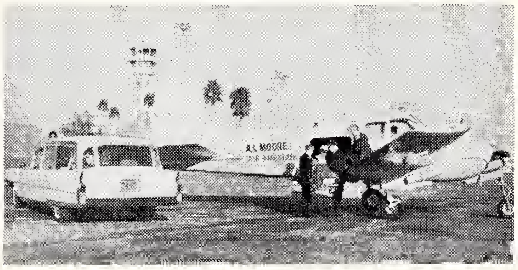

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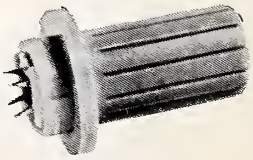

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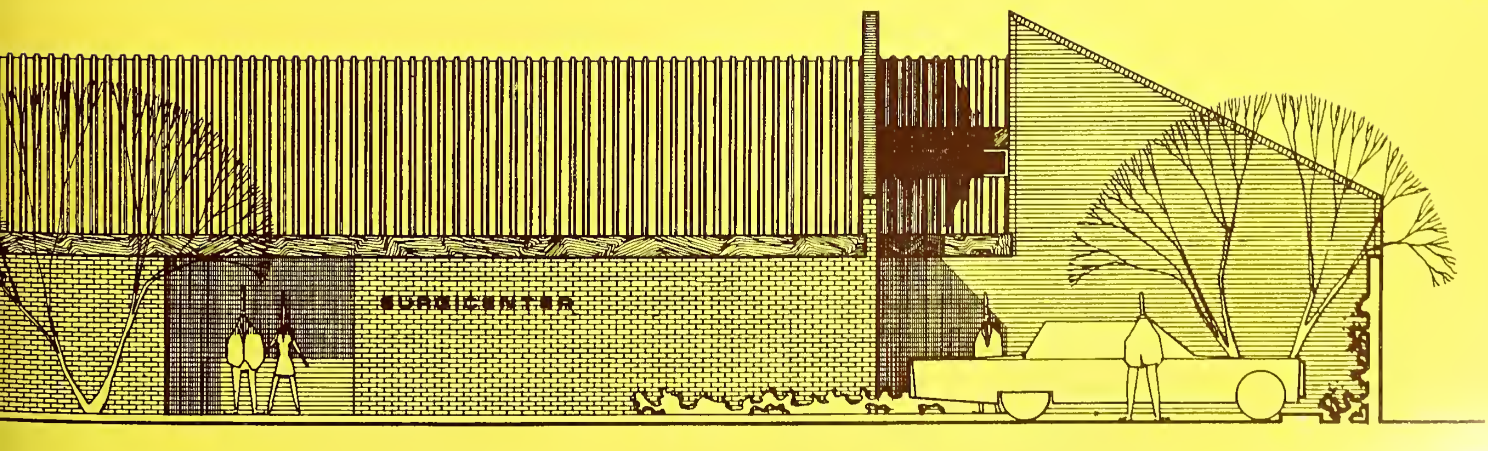

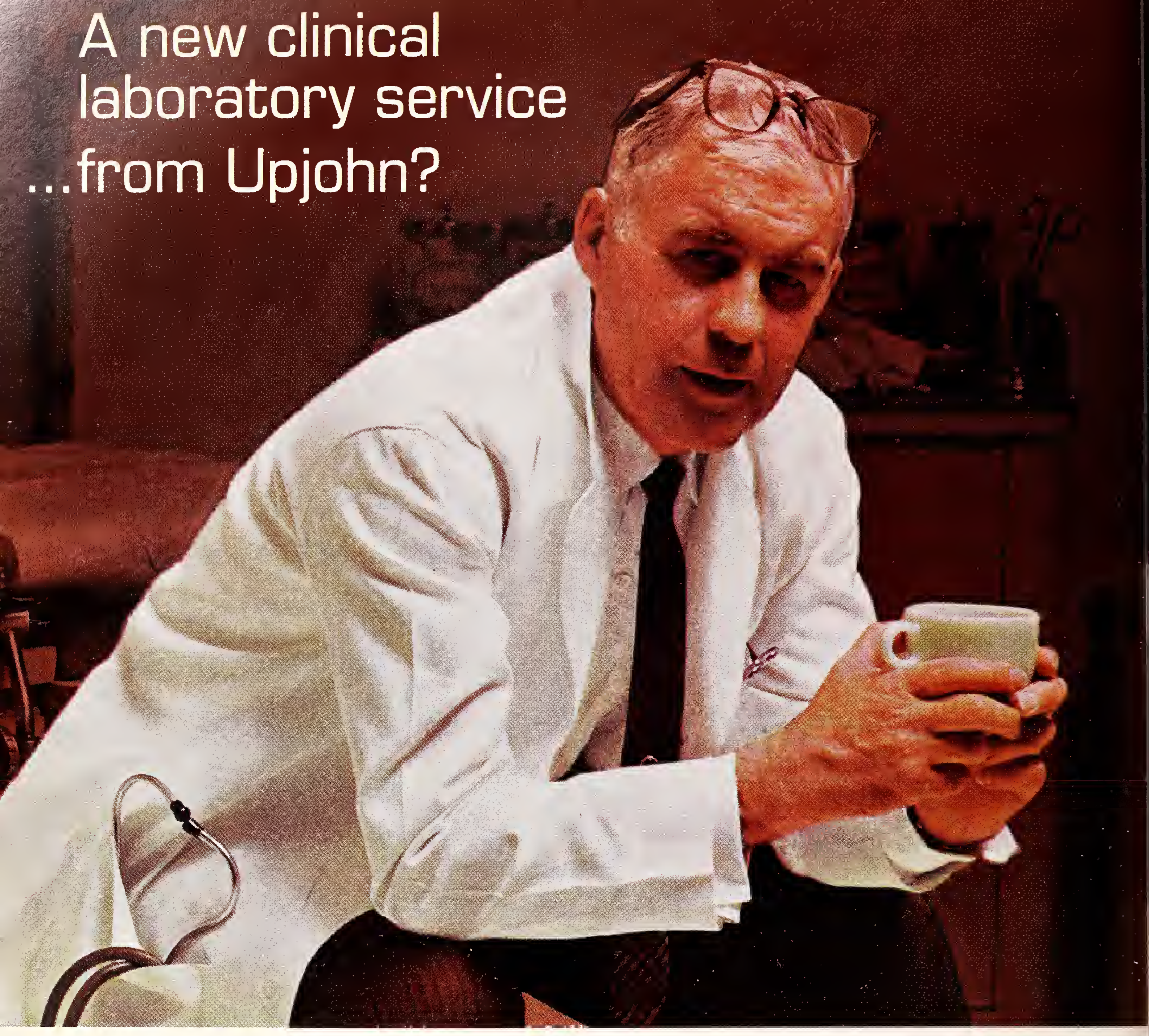
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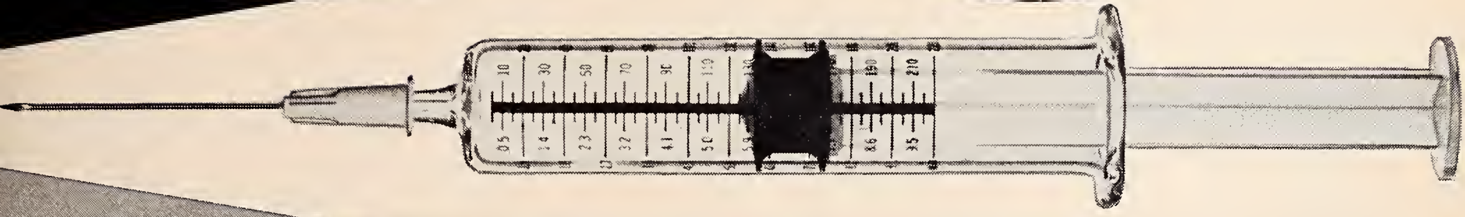

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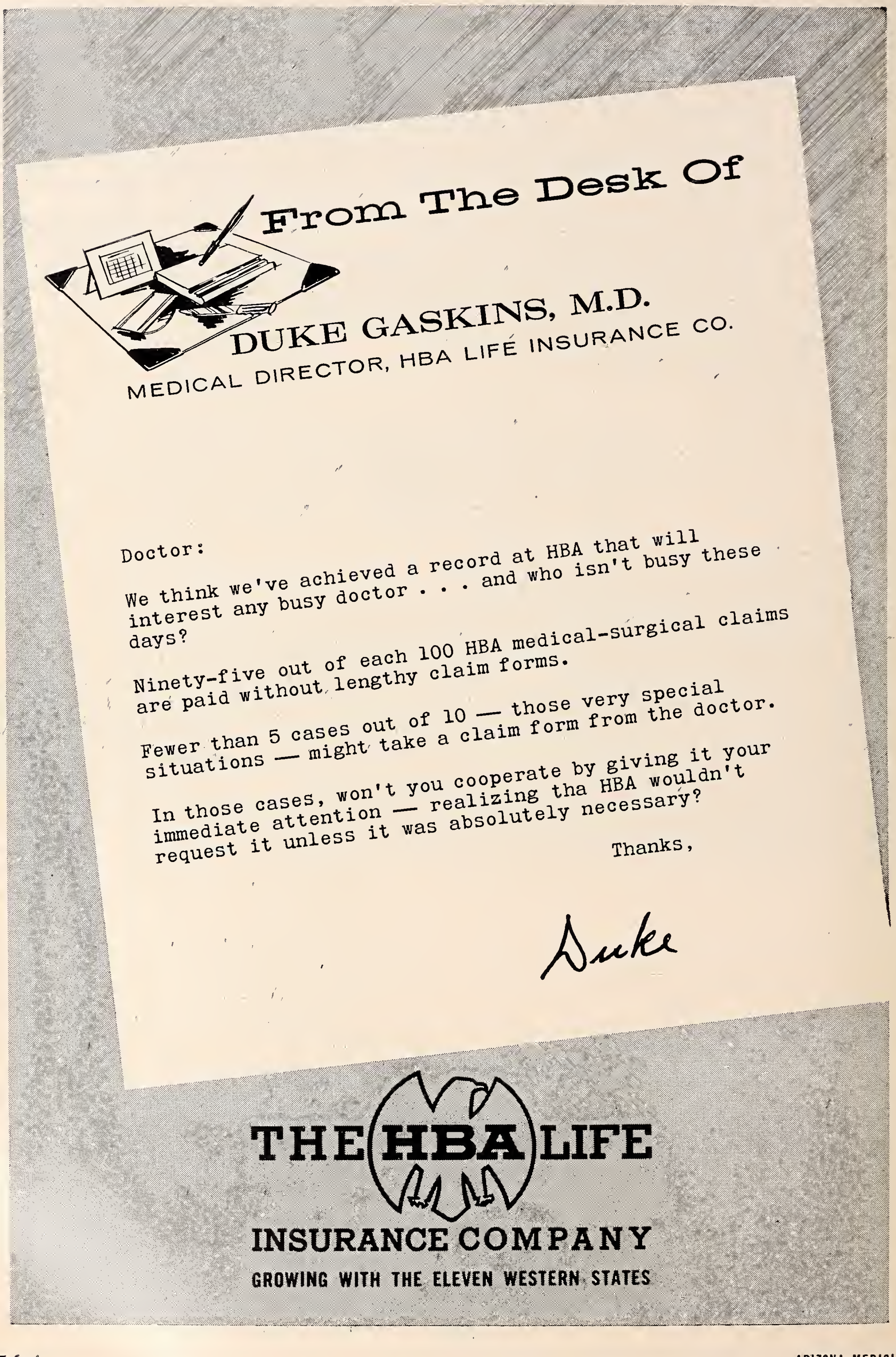

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Published monthly by The Arizona Medical Association, Inc., with offices at 4601 N. Scottsdale Rd., Suite 201, Scottsdale, Arizona 85251. Subscription $5 a year, single copy 50 cents. Second class postage paid at Scottsdale, Arizona, and at additional mailing offices.

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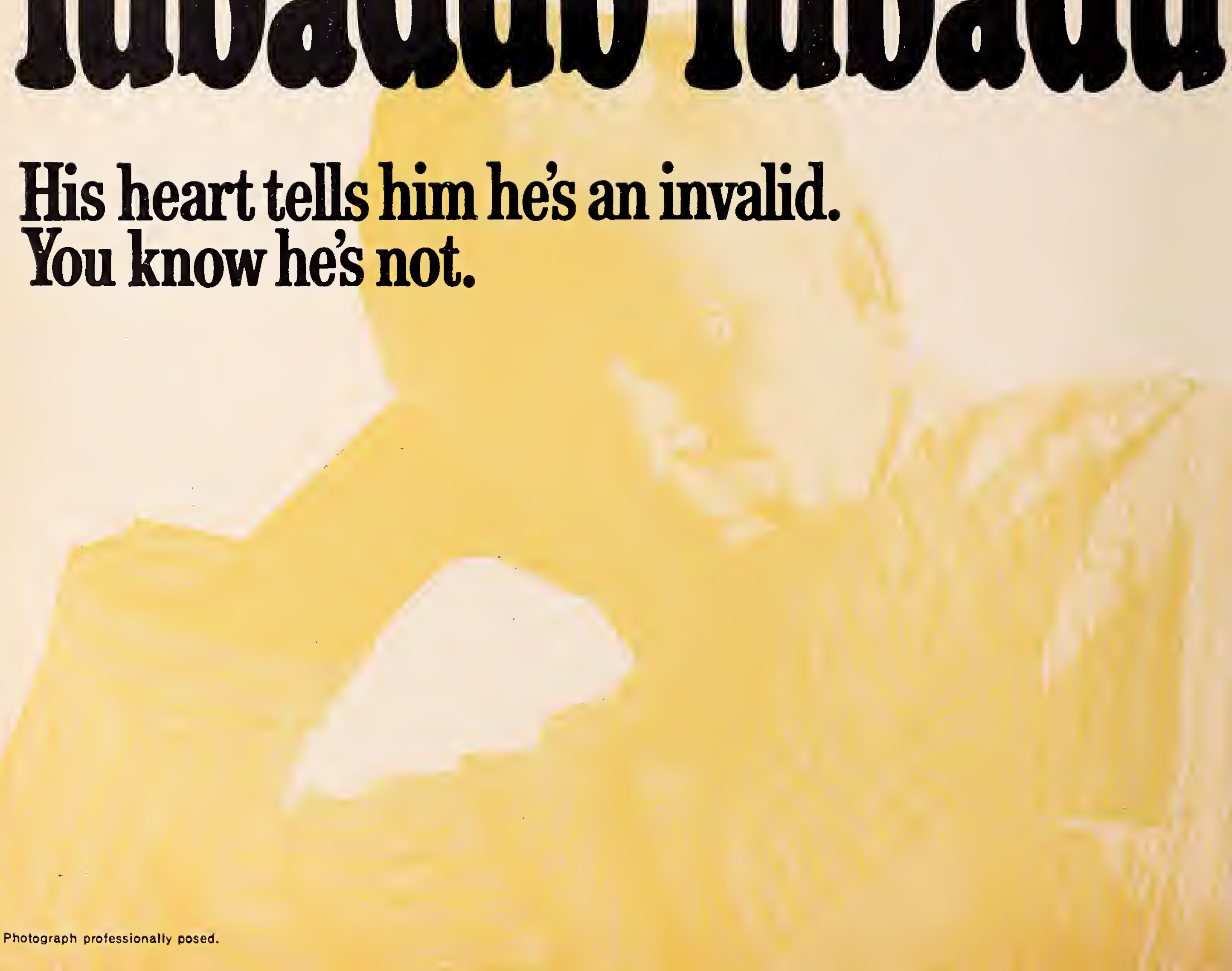

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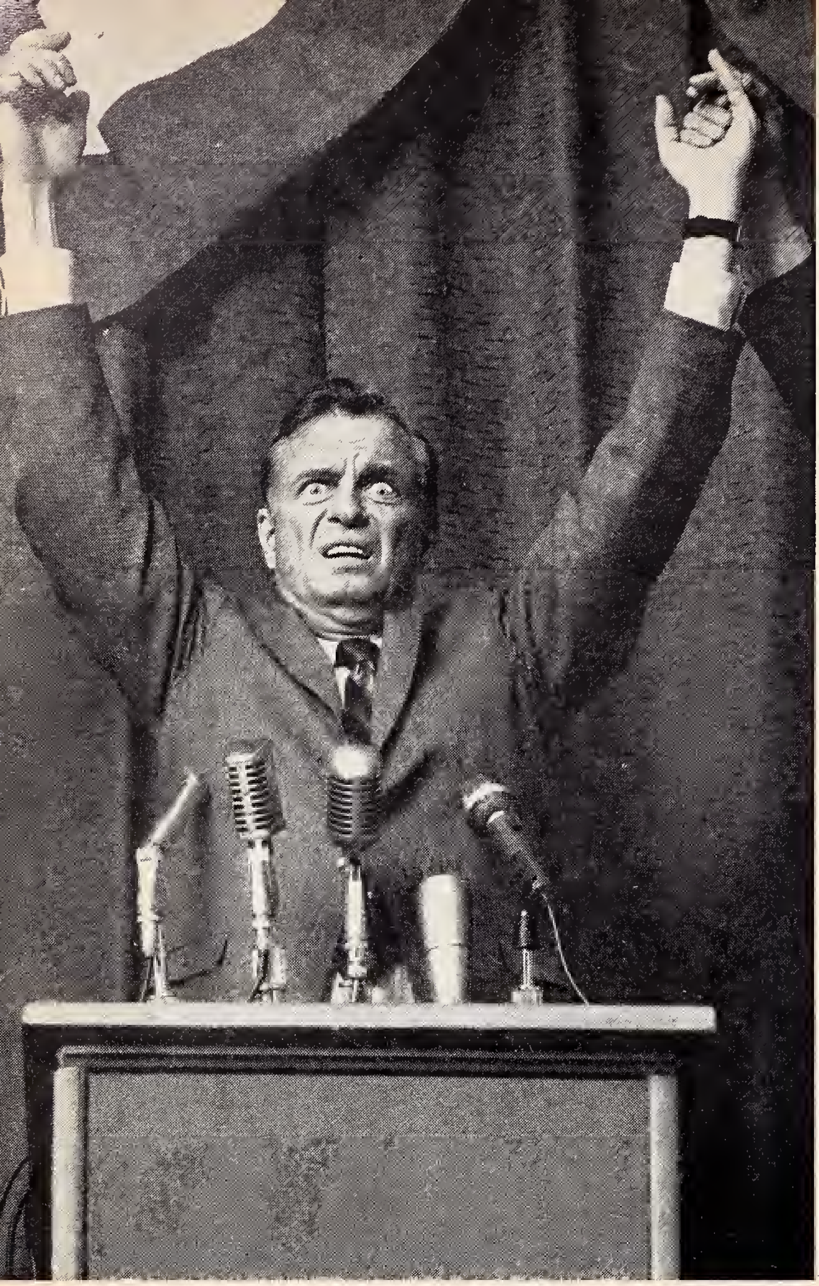

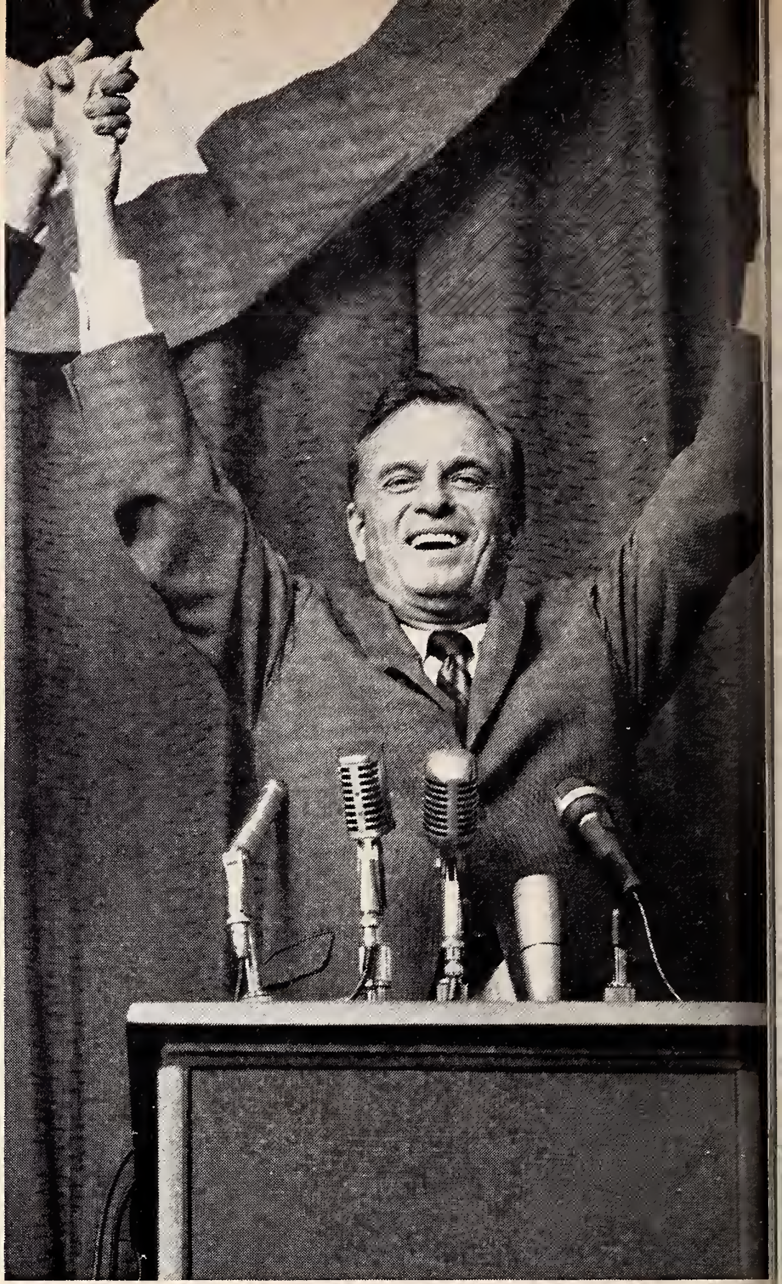

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Editor's Page

CHANGE

"There is a certain relief in change, even though it be from bad to worse as I have found in travelling in a stagecoach, that it is often a comfort to shift ones position and be bruised in a new place." This quote from Washington Irving may be pertinent to the next issue of "Arizona Medicine" which contains an innovation for the members to evaluate.

For the two final issues of this year, the publishing committee has agreed to include an insert called "The Western Journal of Medicine." This insert is prepared by the Journal of the California Medical Association and at their invitation is being included in "**Arizona Medicine.**"

The inclusion of the regional publication costs very little and is designed to enhance the quantity and quality of the scientific material as well as add to the editorial content. Along with these suggested advantages will come some dilution of our own material and a slight loss of the identity of our own state journal.

The present design includes the insert at the beginning of our magazine, with our usual editorial format following. This could be altered.

Arizona Medicine is your Journal and it is up to you, the members, to decide its policy. Unlike some politicians, your editor does not feel that any change is automatically for the better, but rather that altering course should carry with it evidence of improvement. Irving may be right that "There is a certain relief in change . . .," but we want to know if the membership feels that this is an advantageous shift rather than one that will find us ". . . bruised in a new place."

Your letters and comments about this temporary innovation will decide its fate.

Robert F. Lorenzen, M.D.
Editor

The AMBAR® SCRAPBOOK of Obesity Oddities
FACT & LEGEND

OBESITY WAS A MILITARY OFFENSE!
OVERWEIGHT ROMAN HORSEMEN WERE MADE TO FORFEIT THEIR MOUNTS AND BECOME FOOT SOLDIERS!
RECORDED ON AN ENGLISHMAN'S TOMBSTONE
JAMES PARSON
DIED 1743
HE HAD OFTEN EATEN A WHOLE SHOULDER OF MUTTON AND A PECK OF HASTY PUDDING
SHAKESPEARE WAS AWARE OF THE DANGERS OF OBESITY HE WROTE...
Make less thy body hence and more thy grace, leave gormandizing; Know thy grave doth gape for thee wider than for other men.
100 Ambar No. 2 Extentabs
Rx
THE COST OF AMBAR EXTENTABS IS APPROXIMATELY ONE HALF THAT OF OTHER LEADING APPETITE SUPPRESSANTS
AN IMPORTANT FACTOR IN LONG TERM THERAPY

CONTROL FOOD AND MOOD ALL DAY LONG WITH A SINGLE MORNING DOSE

AMBAR #2 EXTENTABS®

methamphetamine HCl 15 mg.,
phenobarbital 64.8 mg. (1 gr.)
(Warning: may be habit forming).

One Ambar Extentab before breakfast can help control most patients' appetite for up to 12 hours. Methamphetamine, the appetite suppressant, gently elevates mood and helps overcome dieting frustrations. Phenobarbital, the sedative in Ambar, controls irritability and anxiety . . helps maintain a state of mental calm and equanimity. Both work together to ease the tensions that erode the willpower during periods of dieting.

Also available: Ambar #1 Extentabs®—methamphetamine hydrochloride 10 mg., phenobarbital 64.8 mg. (1 gr.) (Warning: may be habit forming).

BRIEF SUMMARY/**Indications:** Ambar suppresses appetite and helps offset emotional reactions to dieting. **Contraindications:** Hypersensitivity to barbiturates or sympathomimetics; patients with advanced renal or hepatic disease. **Precautions:** Administer with caution in the presence of cardiovascular disease or hypertension. **Side Effects:** Nervousness or excitement occasionally noted, but usually infrequent at recommended dosages. Slight drowsiness has been reported rarely. See package insert for further details.

A. H. ROBINS COMPANY,
RICHMOND, VA. 23220

A-H-ROBINS

introducing alginates to antacids
for a difference in taste you can feel

Derived from seaweed, and long used to impart velvety consistency to foods, alginates—a Warner-Chilcott contribution to antacid palatability—help 1) erase the chalkiness and grittiness found with some other antacids; 2) dispel unpleasant aftertaste. Like ice cream, Gelusil-M is smooth and creamy; and it has a cool mint flavor. Thus, for your patients Gelusil-M is excellent to start on and easy to stay on.

introducing

GELUSIL®-M NEW

each 5 ml. teaspoonful contains:
500 mg. magnesium trisilicate
250 mg. aluminum hydroxide (Warner-Chilcott)
200 mg. magnesium hydroxide
*U.S. Patent No. 3,326,755

a consistent buffering anticostive† antacid

†Avoids constipation.

See next page for prescribing information ▶

GELUSIL–one name to remember...and a dosage form for every patient.

Gelusil®-M Liquid

Indications: Gelusil-M is indicated for prompt and dependable symptomatic relief of peptic ulcer, gastritis, heartburn, hiatal hernia, esophagitis, and other conditions for which control of gastric hyperacidity is required.

Precaution: Prolonged or intensive therapy in patients with severe renal insufficiency may lead to hypermagnesemia.

Dosage: One to two teaspoonfuls (5 ml. to 10 ml.) between meals and at bedtime or whenever symptoms occur. Certain conditions, such as acute peptic ulcer, may require individualized dosage. If diarrhea occurs, reduce dosage or discontinue use.

Supplied: Gelusil-M (spearmint-flavored)—light green bottles of 12 fl. oz.; and a **special hospital pack.** Keep tightly closed—shake vigorously.

Gelusil® Tablets

Easy to take along / easy to take / pleasantly mint-flavored. An antacid with adsorbent and demulcent properties which contains in one tablet: 0.25 Gm. aluminum hydroxide (Warner-Chilcott) and 0.5 Gm. magnesium trisilicate (USP).

Dosage: 2 tablets—or more—between meals and at bedtime, or whenever symptoms occur. Tablets should be chewed.

Regular Gelusil® Liquid

Pleasant mint flavor...ideal for hospital or home. Available in 12 fl. oz. and 6 fl. oz. bottles and a special hospital pack. An antacid which contains adsorbent and demulcent agents in each 4 ml. teaspoonful: 0.25 Gm. aluminum hydroxide (Warner-Chilcott), 0.5 Gm. magnesium trisilicate (USP).

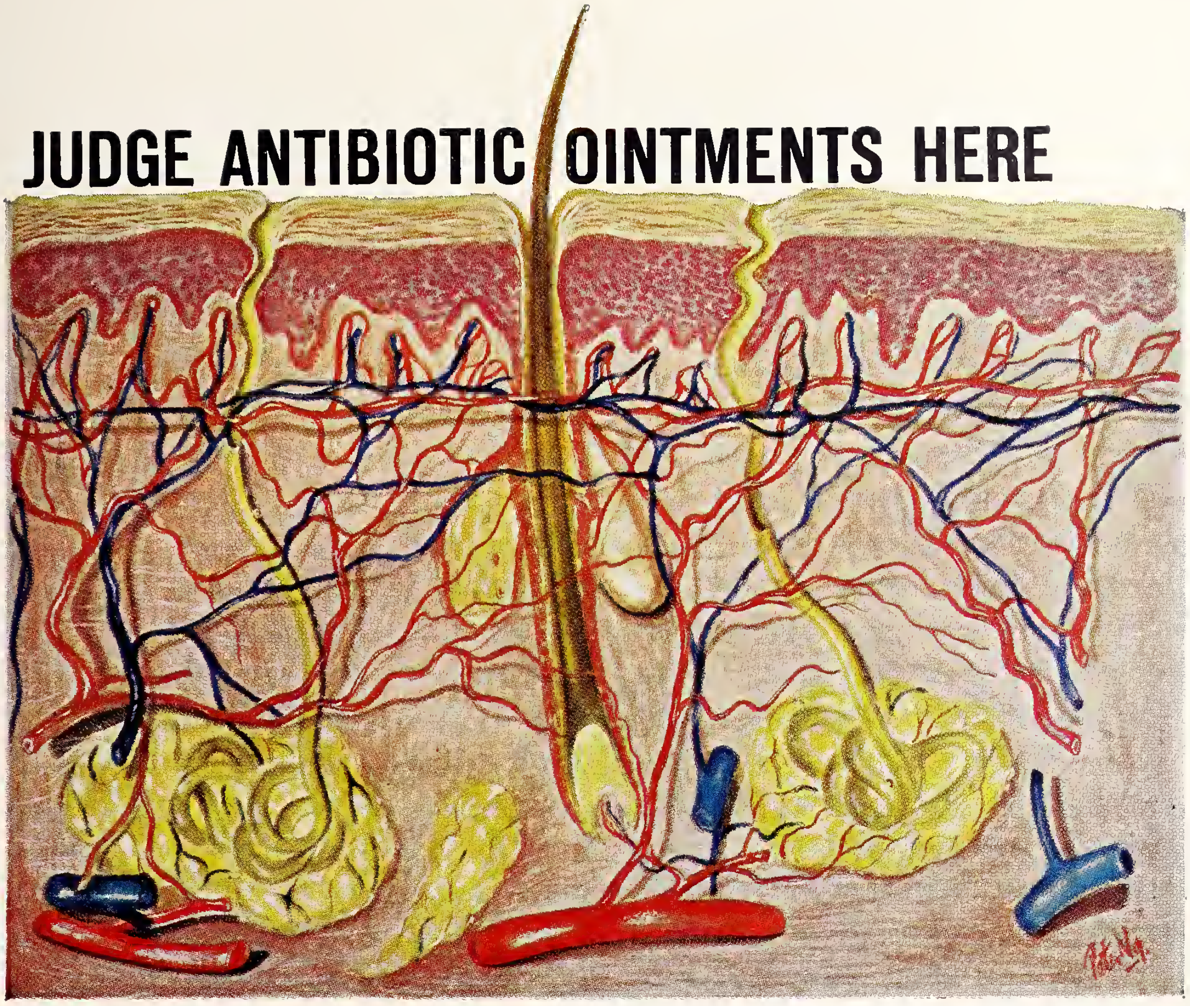
Dosage: 2 teaspoonfuls (4 ml. each)—or more—between meals and at bedtime, or whenever symptoms occur.

Also Available: Gelusil® Flavor-Pack, Gelusil-Lac®.

WC
WARNER-CHILCOTT
Morris Plains, New Jersey

GM-IN-91-4C

JUDGE ANTIBIOTIC OINTMENTS HERE



Results on skin are final proof of any topical antibiotic's effectiveness

No in vitro test can duplicate a clinical situation on living skin. 'Neosporin' (polymyxin B —bacitracin—neomycin) Ointment has consistently proven its effectiveness in thousands of cases of bacterial skin infection. The spectra of the three antibiotics overlap in such a way as to provide bactericidal action against most pathogenic bacteria likely to be found topically. Diffusion of the antibiotics from the special petrolatum base is rapid since they are insoluble in the petrolatum, but readily soluble in tissue fluids. The Ointment is bland and nonirritating.

Caution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

Supplied: Tubes of 1 oz., ½ oz. with applicator tip, and ⅛ oz. with ophthalmic tip.

Complete literature available on request from Professional Services Dept. PML.

'NEOSPORIN'®
brand
POLYMYXIN B-BACITRACIN-NEOMYCIN
OINTMENT

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N.Y.

No place for beginners

Terramycin®
(oxytetracycline)

An infection of rapid onset requiring prompt attention. Teenage girl with chills, fever, abdominal pain, backache and nausea. Frequent and urgent urination with burning. On examination—tenderness over kidney. Blood count and urinalysis confirm the diagnosis: acute pyelonephritis. Treatment is initiated with Terramycin. Within a few days of follow-up therapy, the patient is markedly improved. The pretreatment urine culture shows a strain of *E. coli* highly susceptible to Terramycin.

Experience has shown that Terramycin offers special advantages in treating urinary tract infections when strains of causative bacteria are susceptible. Broad-spectrum coverage unaffected by penicillinase. Effective tissue levels to help reach foci of infection in renal parenchyma. High urine levels—excreted by kidney in *active* form.

With Terramycin, you have the assurance that comes with choosing an agent physicians have depended on for over 18 years. In difficult as well as routine cases, when tests reveal susceptible organisms, consider Terramycin. One of the world's most widely used broad-spectrums.

Contraindicated: In individuals hypersensitive to oxytetracycline.

Warnings: Reduce usual oral dosage and consider antibiotic serum level determinations in patients with impaired renal function.

Use of oxytetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of developing teeth. This effect occurs mostly during long-term use of the drug, but it has also been observed in usual short-treatment courses.

During treatment with tetracyclines, individuals susceptible to photodynamic reactions should avoid direct sunlight; if such reactions occur, discontinue therapy.

Note: With oxytetracycline, phototoxicity is unknown and photoallergy very rare.

Precautions: Use of broad-spectrum antibiotics occasionally may result in overgrowth of nonsusceptible organisms. Where such infections occur, discontinue oxytetracycline and institute specific therapy. Increased intracranial pressure in infants is a possibility. Symptoms disappear upon discontinuation of therapy.

Adverse Reactions: Nausea, diarrhea, glossitis, stomatitis, proctitis, vaginitis and dermatitis, as well as reactions of an allergic nature, may occur but are rare.

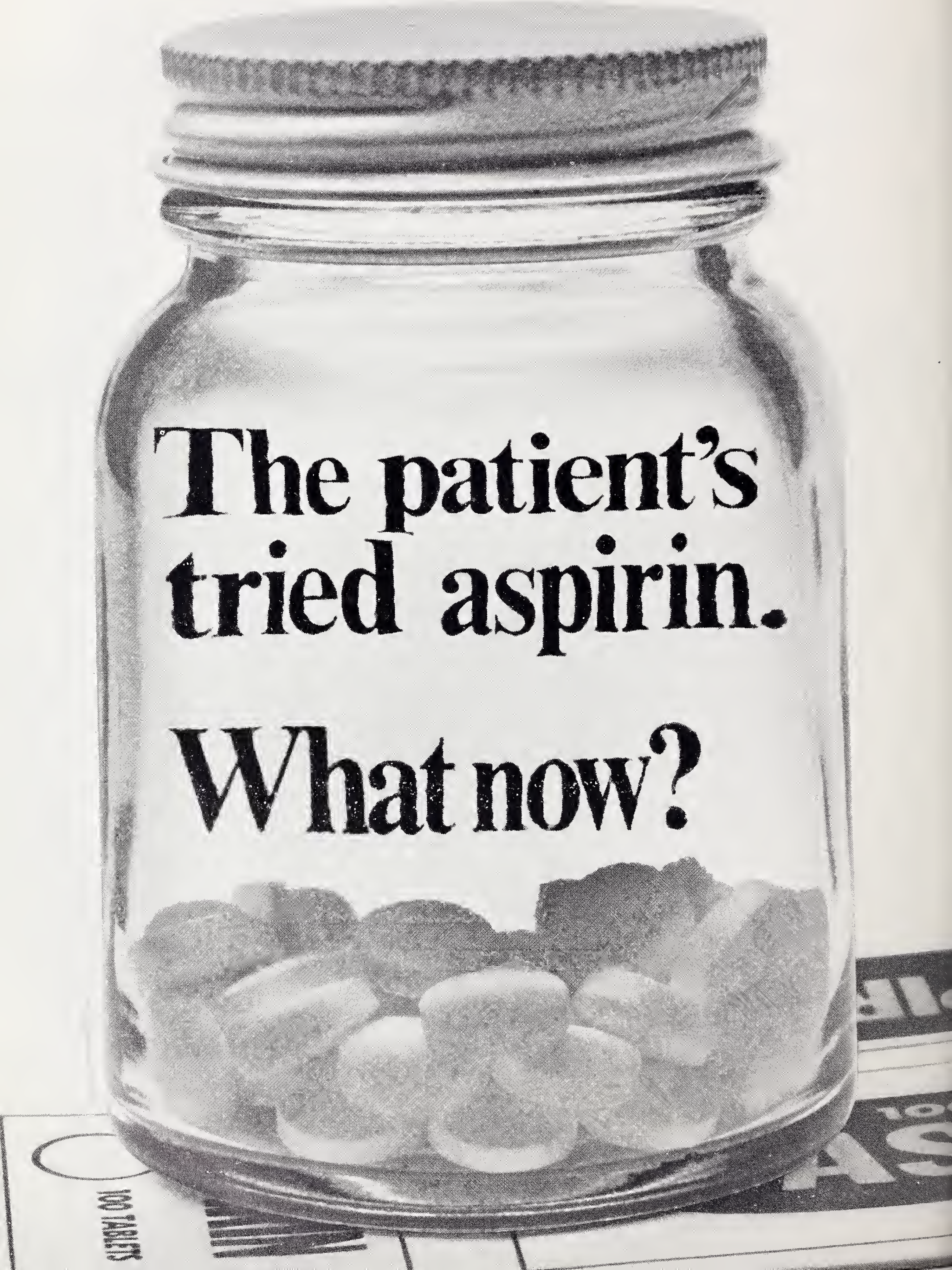
Supply:* Terramycin Capsules: oxytetracycline HCl, 250 mg. and 125 mg. Terramycin Syrup: calcium oxytetracycline, 125 mg. per 5 cc. Terramycin Pediatric Drops: calcium oxytetracycline, 100 mg. per cc.

*All potencies listed are in terms of the standard, oxytetracycline.

More detailed professional information available on request.

Terramycin®
(oxytetracycline)

Pfizer **LABORATORIES DIVISION**
New York, N.Y. 10017


The patient's tried aspirin.
What now?
100 TABLETS

There's a good chance your patient needs more than a non-prescription analgesic for pain relief. Especially after self-medication has failed.

Because continuing, increased pain and discomfort may in part be a reflection of anxiety, Equagesic is worthy of consideration. In a single, non-narcotic preparation, it helps relieve pain . . . *and* associated anxiety and tension.

Tablets
Equagesic®
(meprobamate and ethoheptazine citrate with aspirin) Wyeth

IN BRIEF

Contraindications: History of sensitivity or severe intolerance to aspirin, meprobamate or ethoheptazine citrate.

Warnings: USE IN PREGNANCY: Safety for use during pregnancy or lactation has not been established; therefore, it should be used in pregnant patients or women of child-bearing age only when the physician judges its use essential to the patient's welfare.

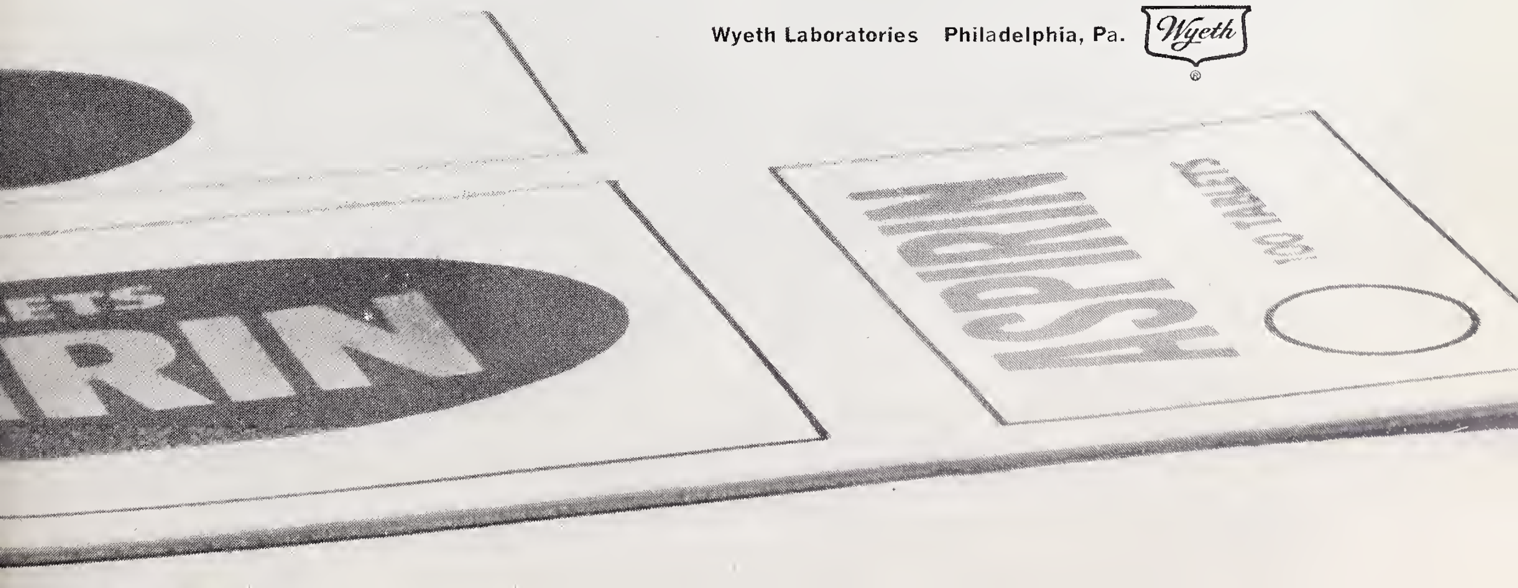
Precautions: Keep out of reach of children. Not recommended for patients 12 years old or less. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate in susceptible persons—as alcoholics, ex-addicts, severe psychoneurotics—has resulted in dependence or habituation. Withdraw gradually after prolonged excessive dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance, with resultant slowed reactions and impaired judgment and coordination. If drowsiness, ataxia or visual disturbances (impairment of accommodation and visual acuity) occur, reduce dose. If symptoms persist, patients should not operate machinery or drive. After meprobamate overdose, prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels, and hyperventilation are reported. Give cautiously and in small amounts to patients with suicidal tendencies. Treat attempted suicide (has resulted in coma, shock, vasomotor and respiratory collapse and anuria) with gastric lavage and appropriate symptomatic therapy (CNS stimulants and pressor amines as indicated). Two instances of accidental or intentional significant overdosage with ethoheptazine and aspirin have been reported. These were accompanied by CNS depression (drowsiness and lightheadedness) but resulted in uneventful recovery. On basis of pharmacologic data, CNS stimulation could be anticipated, with nausea, vomiting and salicylate intoxication (requires induced vomiting or gastric lavage, specific parenteral electrolyte therapy for ketoacidosis and dehydration, and observation for hypoprothrombinemic hemorrhage [usually requires whole blood transfusions]).

Adverse Reactions: Ethoheptazine and aspirin may cause nausea with or without vomiting and epigastric distress in a small percentage of patients. Dizziness is rare at recommended dosage. Meprobamate may cause drowsiness, ataxia and rarely allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses. Such patients may have had no previous contact with meprobamate and may or may not have an allergic history. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. If allergic reaction occurs, discontinue meprobamate; do not reinstitute. Severe reactions, observed very rarely, include fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. These cases should be treated symptomatically including, when indicated, such medication as epinephrine, antihistamine and possibly hydrocortisone. A few cases of leukopenia, usually transient, have been reported on continuous use. Rarely, aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported, almost always in presence of known toxic agents.

Overdosage: See precautions section for management of overdosage.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

Wyeth Laboratories Philadelphia, Pa. Wyeth®



They don't feel they "suffer" from hypertension...

that's the "Buti" part of Butiserpazide.

The "Buti" part of BUTISERPAZIDE—the mildly sedative action of BUTISOL acting in concert with the classic thiazide/reserpine formula—proved helpful in one study in reducing hypertensive symptoms in over half the patients.[1]

Among the symptoms showing "striking" overall improvement were headache, nervousness, palpitation and dizziness. Nor is that all there is to the "beauty" of BUTISERPAZIDE. Clinical comparisons have also shown that many patients respond with smooth, uniform lowering of blood pressure[2]... at times *below* the levels achieved with previous therapy[1,2]... as well as a lowered incidence of drug side effects. (The usual dosage is just 1 tablet once or twice a day.)

You have a choice of 2 strengths:

Butiserpazide®-25

PRESTABS®* Tablets
BUTISOL® (butabarbital) 30 mg.†; hydrochlorothiazide 25 mg.; reserpine 0.1 mg.

Butiserpazide®-50

PRESTABS®* Tablets
BUTISOL® (butabarbital) 30 mg.†; hydrochlorothiazide 50 mg.; reserpine 0.1 mg.

Lowers blood pressure so smoothly that patients are often untroubled by either the disease... or therapy

Contraindications: Sensitivity to any component, porphyria, peptic ulcer, ulcerative colitis, mental depression, renal impairment or shutdown. **Warnings:** Consider the possibility of sensitivity reactions in patients with history of allergy or bronchial asthma. Coated potassium tablets, sometimes administered in conjunction with antihypertensive therapy, may be associated with small bowel lesions, which have led to obstruction, hemorrhage and perforation. Surgery has frequently been required and deaths have occurred. Such tablets should be used only when indicated and when adequate dietary supplementation is not practical. They should be discontinued immediately if abdominal pain, distention, nausea, vomiting, or g.i. bleeding occur. *Use in Pregnancy:* Exercise caution, since thiazides cross the placental barrier and may cause fetal or neonatal hyperbilirubinemia, thrombocytopenia or altered carbohydrate metabolism; adverse reactions seen in the adult may occur in the newborn. Use reserpine in women of childbearing age only when essential to patient welfare. Increased respiratory secretions, nasal congestion, cyanosis, and anorexia may occur in infants born to reserpine-treated mothers. **Precautions:** *Butisol* (butabarbital)—Exercise caution in moderate to severe hepatic disease. Elderly or debilitated patients may react with marked excitement or depression. *Hydrochlorothiazide*—May induce electrolyte imbalance; when used with digitalis or one of its glycosides and in patients with severe hepatic insufficiency, cardiac arrhythmias or symptoms of impending hepatic coma may occur. Discontinue and institute appropriate countermeasures if prolonged use produces hypokalemia or (likely with sodium restriction) hyponatremia and hypochloremic alkalosis. (Ammonium chloride, used to reverse hypochloremic alkalosis, is contraindicated in hepatic disease.) May produce elevated serum uric acid levels (and, infrequently, gout) or reduce glucose tolerance, altering insulin requirements in diabetics. *Reserpine*—Observe for signs or symptoms of peptic ulcer or ulcerative colitis. Discontinue at first sign of mental depression; keep in mind possibility of suicide. Exercise extreme caution in history of mental depression. May produce cardiac arrhythmias when used with digitalis and quinidine, or may precipitate biliary colic in patients with gallstones. Discontinue 1 to 2 weeks before surgery; inform the anesthetist in event of emergency surgery. Exercise caution in history of epilepsy. Discontinue 1 to 2 weeks before ECT. *General*—Exercise caution in coronary artery disease. **Adverse Reactions:** Dizziness, drowsiness, weakness, nasal congestion, leg cramps, nausea, palpitations, superficial skin bruises, palmar erythema, headache, dehydration, skin rash, "hangover," systemic disturbances, diarrhea, itching, vomiting, paresthesia, photosensitivity, pancreatitis, jaundice, xanthopsia, purpura, thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, anorexia, gastric irritation, abdominal cramping, constipation, glycosuria, vertigo, cutaneous vasculitis, orthostatic hypotension (potentiated by alcohol, barbiturates, or narcotics), increased salivation and gastric secretion, increased intestinal motility, loose stools, angina-like syndrome, arrhythmias, bradycardia, flushing, hypotension, nervousness, paradoxical anxiety, rarely atypical Parkinsonian syndrome, central nervous system sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, optic atrophy), dryness of mouth, syncope, epistaxis, weight gain, and impotence or decreased libido. **Usual Adult Dosage:** BUTISERPAZIDE®-25 or BUTISERPAZIDE®-50: 1 tablet daily or b.i.d. When used with other antihypertensive agents reduce dosage of both drugs about 50% and observe carefully for changes in blood pressure. *Before prescribing or administering, see package insert.* **References:** 1. Coodley, E. L.: Curr. Ther. Res. 4:460 (Sept.) 1962. 2. Johnson, H. J., Jr.: Penn. Med. J. **67**:35 (May) 1964.

McNEIL

McNeil Laboratories, Inc.
Fort Washington, Pa. 19034

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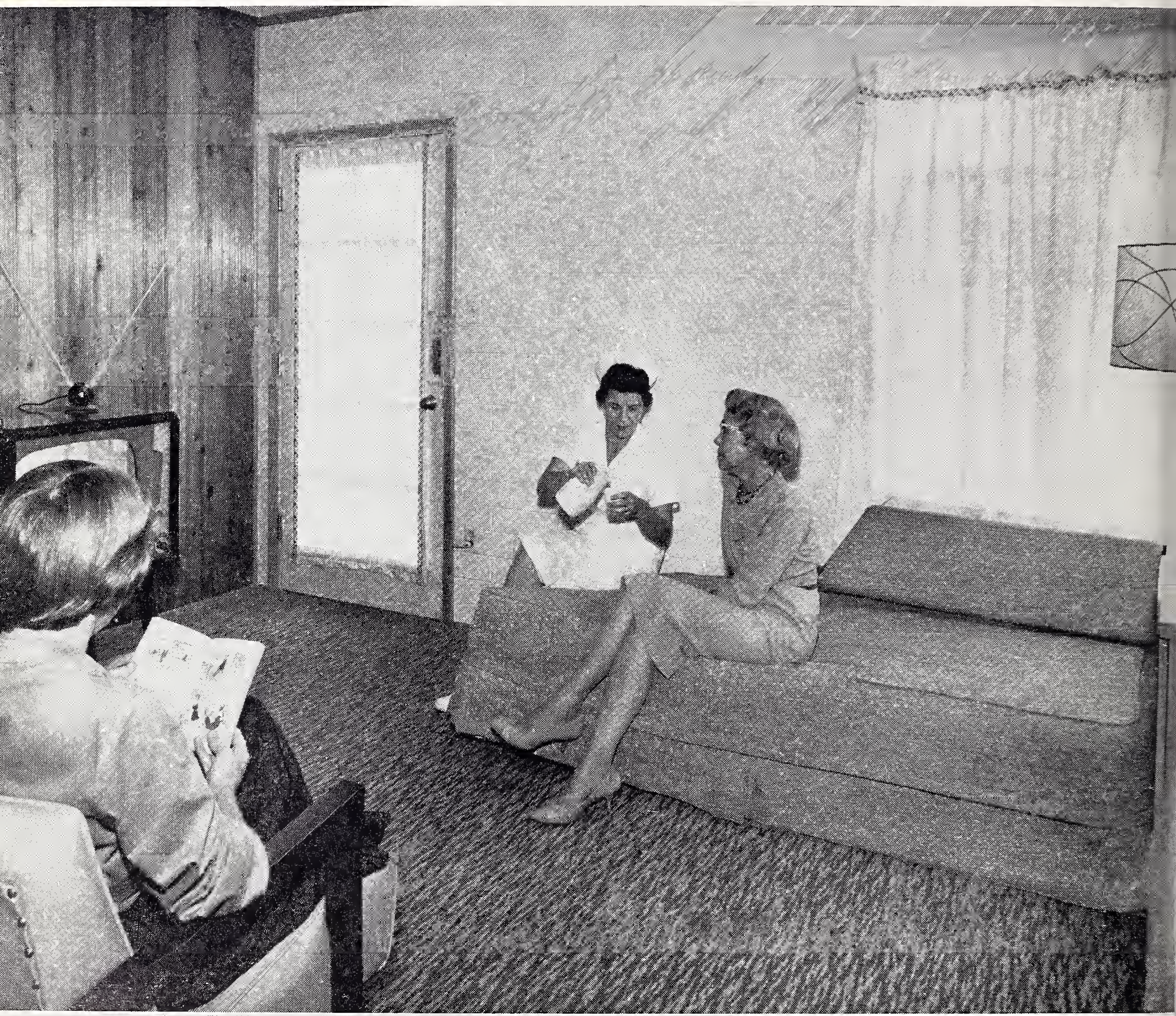
†Warning: May be habit forming.

*15 mg. of BUTISOL (butabarbital), plus the other ingredients, in outer layer; 15 mg. of BUTISOL in a specially coated core for delayed release, to approximately equalize duration of action for all components.

Constant care, supervision and companionship are an integral part of the therapy program at Camelback Hospital. Whether patients prefer restful hobbies such as TV viewing, reading, conversing in the modern, comfortable rooms, or enjoy more active out-of-doors recreation, highly-trained, registered nurses are always nearby.



Located in the heart of the beautiful Phoenix citrus area near picturesque Camelback Mountain, the hospital is dedicated exclusively to the treatment of psychiatric and psychosomatic disorders, including alcoholism.

PPROVED BY THE JOINT COMMISSION ON ACCREDITATION
F HOSPITALS; and THE AMERICAN PSYCHIATRIC ASSOCIATION

Camelback Hospita

5055 North 34th Stree
955-6200
PHOENIX, ARIZON
ARIZONA FOUNDATION FOR NEUROLOGY AND PSYCHIATR
A Non-Profit Corporatio

If she asks what you think of babyScott

The next page will help you answer.

Introducing the babyScott diaper system. Designed with infants, mothers, and physicians in mind.

Two-part system offers clinical advantages as well as convenience and efficiency.

The diaper panty: it takes anatomy into consideration. The babyScott diaper panty is specifically designed to hold the babyScott disposable diaper securely, yet without constriction. The panty fits low in front to avoid pressure on the umbilicus. And high on the legs so it won't chafe, bind or interfere with mobility.

Four different sizes and multi-position snaps help assure good fit and comfort. "Safety" pins, which can always pose a threat, are completely unnecessary.

All portions of the panty that come in contact with the infant's skin are covered with soft, quick-drying cloth.

Essentially non-absorbent, the babyScott panty can be thoroughly and rapidly washed, rinsed and dried.

The disposable diaper: it takes sensitive skin into consideration. The disposable diaper, itself, is thick, fluffy and soft. Its layers of highly absorbent cellulose fluff are covered by a web-like liner, which is both permeable and relatively hydrophilic to help keep infants drier.

Doubly thick for extra absorption in front, the diaper fans out bucket-seat fashion in the back for wide coverage. The babyScott diaper thus provides excellent protection while minimizing bunching and consequent irritation. On those occasions when double diapers are used for extra protection comfort is still maintained.

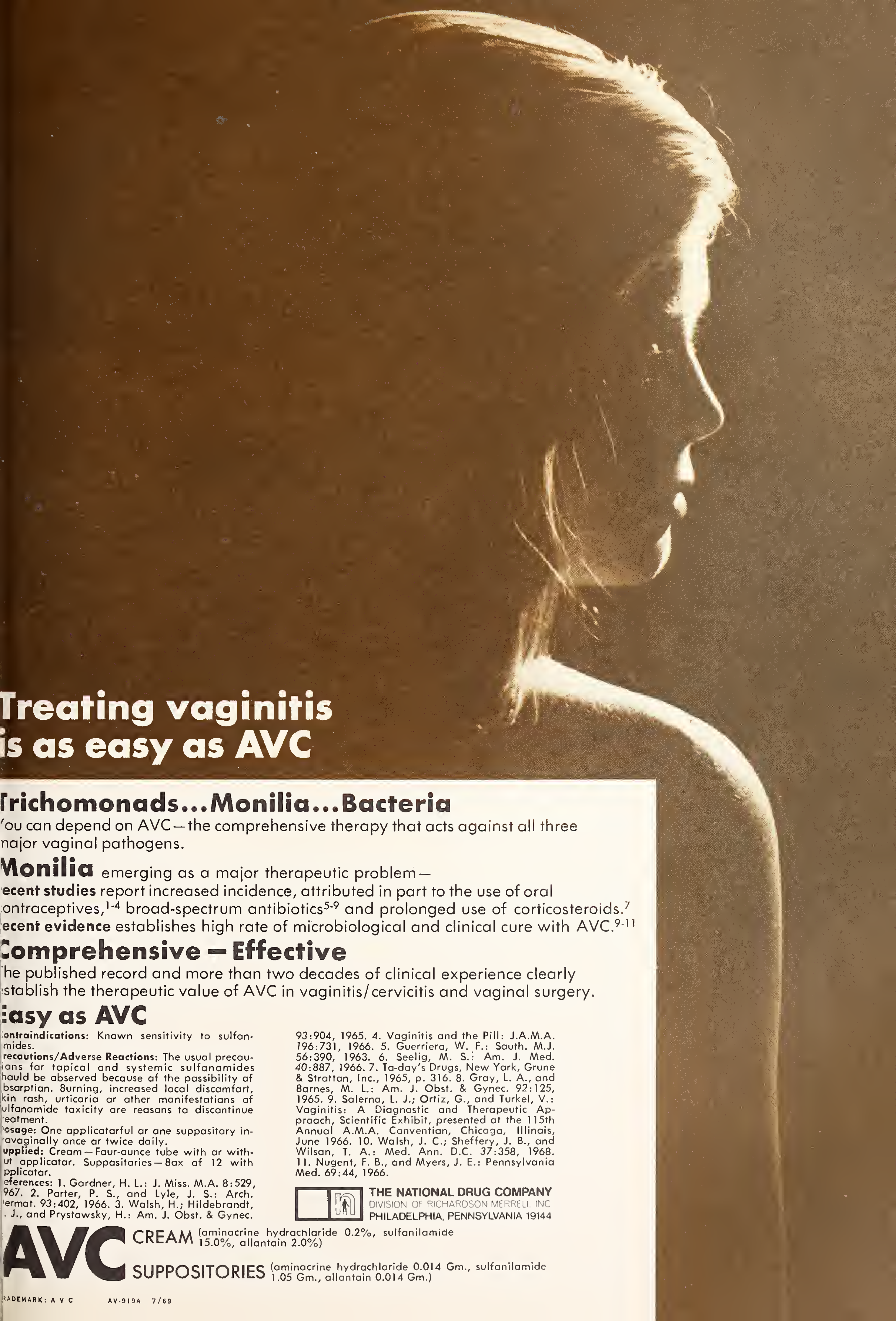
With babyScott, each diaper comes fresh and clean out of the pack. It's used only once, then flushed away or otherwise disposed of.

No soap, detergent or bleach residues. No opportunity for cross contamination from the diaper.

A frequently changed infant is a healthier, happier infant.
And the babyScott diaper system is so easy to use, it will be used.

babyScott®
the pinless diaper

Another fine quality product from Scott Paper Company



Treating vaginitis is as easy as AVC

Trichomonads...Monilia...Bacteria

ou can depend on AVC — the comprehensive therapy that acts against all three najor vaginal pathogens.

Monilia emerging as a major therapeutic problem —

ecent studies report increased incidence, attributed in part to the use of oral ontraceptives,[1-4] broad-spectrum antibiotics[5-9] and prolonged use of corticosteroids.[7]
ecent evidence establishes high rate of microbiological and clinical cure with AVC.[9-11]

Comprehensive — Effective

he published record and more than two decades of clinical experience clearly stablish the therapeutic value of AVC in vaginitis/cervicitis and vaginal surgery.

Easy as AVC

ontraindications: Known sensitivity to sulfon- mides.
recautions/Adverse Reactions: The usual precau- ians for topical and systemic sulfonamides hould be observed because of the possibility of bsorption. Burning, increased local discomfort, kin rash, urticaria or other manifestations of ulfonamide toxicity are reasons to discontinue eatment.
osage: One applicatorful or one suppository in- avaginally once or twice daily.
upplied: Cream — Four-ounce tube with or with- ut applicator. Suppositories — Box of 12 with pplicator.
eferences: 1. Gardner, H. L.: J. Miss. M.A. 8:529, 967. 2. Porter, P. S., and Lyle, J. S.: Arch. ermat. 93:402, 1966. 3. Walsh, H.; Hildebrandt, . J., and Prystawsky, H.: Am. J. Obst. & Gynec. 93:904, 1965. 4. Vaginitis and the Pill: J.A.M.A. 196:731, 1966. 5. Guerriero, W. F.: South. M.J. 56:390, 1963. 6. Seelig, M. S.: Am. J. Med. 40:887, 1966. 7. To-day's Drugs, New York, Grune & Stratton, Inc., 1965, p. 316. 8. Gray, L. A., and Barnes, M. L.: Am. J. Obst. & Gynec. 92:125, 1965. 9. Salerno, L. J.; Ortiz, G., and Turkel, V.: Vaginitis: A Diagnostic and Therapeutic Approach, Scientific Exhibit, presented at the 115th Annual A.M.A. Convention, Chicago, Illinois, June 1966. 10. Walsh, J. C.; Sheffery, J. B., and Wilson, T. A.: Med. Ann. D.C. 37:358, 1968. 11. Nugent, F. B., and Myers, J. E.: Pennsylvania Med. 69:44, 1966.

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON MERRELL INC
PHILADELPHIA, PENNSYLVANIA 19144

AVC CREAM (aminacrine hydrochloride 0.2%, sulfanilamide 15.0%, allantoin 2.0%)
SUPPOSITORIES (aminacrine hydrochloride 0.014 Gm., sulfanilamide 1.05 Gm., allantoin 0.014 Gm.)

ADEMARK: A V C AV-919A 7/69

Painful night leg cramps...

unwelcome bedfellow for any patient–including those with arthritis, diabetes or PVD

One thing patients can sleep without, particularly patients with chronic disease conditions such as arthritis, diabetes or PVD, is painful night leg cramps. Although seldom the presenting complaint, night leg cramps can tie your patients up in painful knots. Now, just one tablet of QUINAMM at bedtime can usually bring an end to shattered sleep and needless suffering. Your patients will sleep restfully—gratefully—with QUINAMM, specific therapy to prevent painful night leg cramps.

Prescribing Information—Composition: Each white, beveled, compressed tablet contains: Quinine sulfate, 260 mg., Aminophylline, 195 mg. **Indications:** For the prevention and treatment of nocturnal and recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis and static foot deformities. **Contraindications:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions/Adverse Reactions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets.

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON-MERRELL INC.
PHILADELPHIA, PENNSYLVANIA 19144

Quinamm™ Specific therapy for night leg cramps
(quinine sulfate 260 mg., aminophylline 195 mg.)

FIRST LADY OF THE LAND.

So noble. So majestic. And, she's got a right to be. She gives Nature's finest. Pure, whole milk.

Milk to grow on. Milk to stay strong on. Real milk, Nature's most healthful food.

You may think most people know all about milk. Unfortunately, many don't.

They don't know that milk contains all the nutrients known to be needed by humans. Essential amino acids and essential fatty acids. And, too, milk contains over 140 fatty acids, and is easily digestible.

Someone should explain milk's vital role in a balanced diet of meat, breads and cereals, fruits and vegetables and dairy foods.

We hope you will do the explaining. As a professional, people will listen to you.

We'd like to help you with the facts. We have complete materials available for you to read or let others read. They're all free.

If you have a free minute, send for them.

The Real Milk Story

Dairy Council of Arizona
1016 North 32nd Street
Phoenix, Arizona 85008

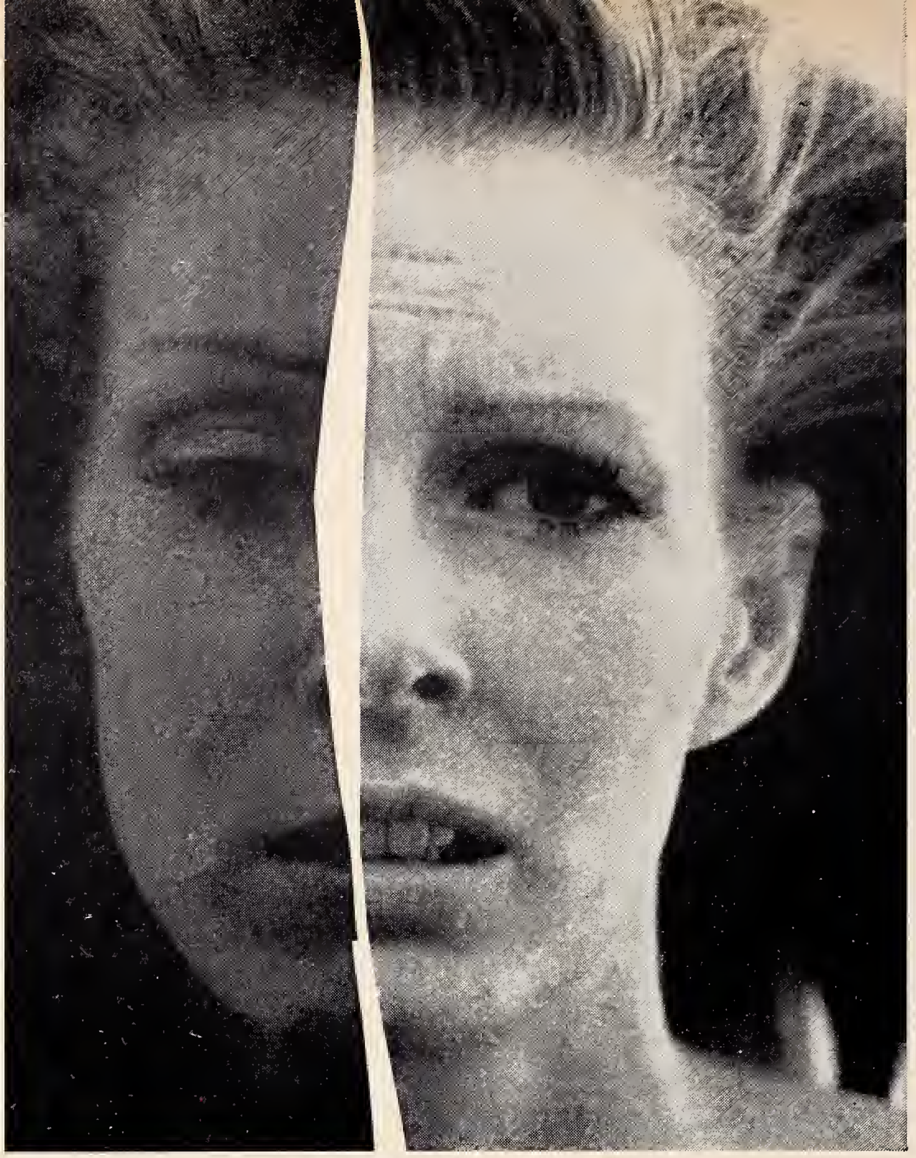
Name ________________________

Position ________________________

Address ________________________

City ________________________

State ____________ Zip



symptoms of mixed anxiety-depression are rarely clear-cut...

but they are often a clear indication for

Mellaril®

(thioridazine)

25 mg. t.i.d.

effective in mixed anxiety-depression and in moderate to severe anxiety

Before prescribing or administering, see Sandoz literature for full product information, including adverse reactions reported with phenothiazines. The following is a brief precautionary statement.

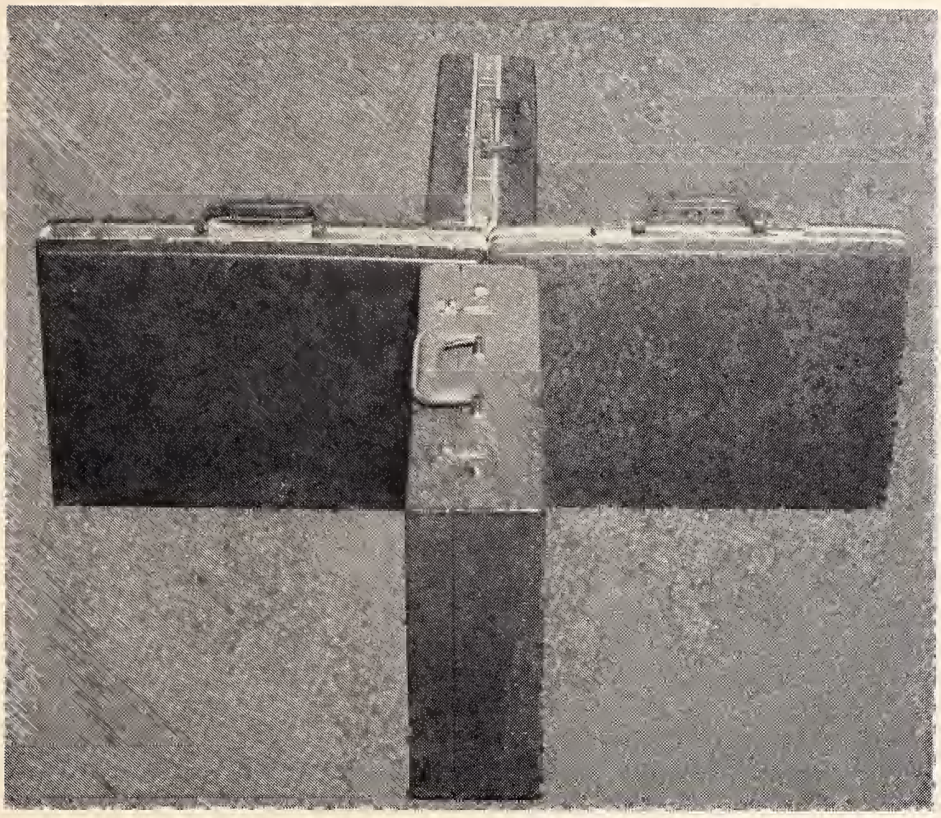
Contraindications: Severe central nervous system depression, comatose states from any cause, hypertensive or hypotensive heart disease of extreme degree.

Warnings: Administer cautiously to patients who have previously exhibited a hypersensitivity reaction (e.g., blood dyscrasias, jaundice) to phenothiazines. Phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus insecticides. During pregnancy, administer only when necessary.

Precautions: There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures. In epileptic patients, anticonvulsant medication should also be maintained. Pigmentary retinopathy may be avoided by remaining within the recommended limits of dosage. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving). Orthostatic hypotension is more common in females than in males. Do not use epinephrine in treating drug-induced hypotension. Daily doses in excess of 300 mg. should be used only in severe neuropsychiatric conditions.

Adverse Reactions: *Central Nervous System*—Drowsiness, especially with large doses, early in treatment; infrequently, pseudoparkinsonism and other extrapyramidal symptoms; nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. *Autonomic Nervous System*—Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. *Endocrine System*—Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. *Skin*—Dermatitis and skin eruptions of the urticarial type, photosensitivity. *Cardiovascular System*—Changes in the terminal portion of the electrocardiogram have been observed in some patients receiving the phenothiazine tranquilizers, including Mellaril (thioridazine). While there is no evidence at present that these changes are in any way precursors of any significant disturbance of cardiac rhythm, several sudden and unexpected deaths apparently due to cardiac arrest have occurred in patients previously showing electrocardiographic changes. The use of periodic electrocardiograms has been proposed but would appear to be of questionable value as a predictive device. *Other*—A single case described as parotid swelling.

SANDOZ PHARMACEUTICALS, HANOVER, N.J. SANDOZ 69-384



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ArMA Reports

THE MINUTES APPEARING IN THIS SECTION HAVE BEEN EDITED TO CONSERVE SPACE. A COMPLETE COPY OF THE MINUTES OF ANY MEETING WILL BE MAILED TO ANY MEMBER REQUESTING THEM.

BENEVOLENT AND LOAN FUND COMMITTEE

Meeting of the Benevolent and Loan Fund Committee of the Arizona Medical Association, Inc., held Sunday, August 24, 1969 in the Central Office of the Association, Suite 201, Safari Building, 4601 North Scottsdale Road, Scottsdale, Arizona, convened at 10:05 a.m., Daniel T. Cloud, M.D., Chairman, presiding.

ROLL CALL

PRESENT: Drs. Chloupek, William N.; Cloud, Daniel T., Chairman; Dew, Philip E., Treasurer; DuVal, Jr., Merlin K.; Landeen, Fred H., President-Elect.

STAFF: Messrs. Carpenter, Robert, Executive Director; Robinson, Bruce E., Assistant Executive Director.

EXCUSED: Drs. Boiko, George; Flynn, Richard O., President; Sattenspiel, Edward, Secretary.

MINUTE

Approved minute of the meeting of the Benevolent and Loan Fund Committee held July 28, 1968.

FINANCES

Scholarship Fund

The 1969 Budget appropriated $5,100.00 to the Scholarship Fund. Expended to July 31, 1969 a sum of $2,074.64, reflecting balance of $3,025.36. The Scholarship Fund in trust as of July 31, 1969, reflects a balance of $14,157.32.

Benevolence Fund

The Benevolence Fund in trust reflects a balance as of July 31, 1969, of $14,339.22. The Board of Directors of this Association in meeting held November 10, 1968, account illness and hardship, authorized a monthly payment of $152.50 commencing October 1, 1968, toward the infirmary maintenance of the widow of Eldon Charvoz, deceased, to be financed out of the Benevolence Fund, a like sum being contributed by the Maricopa County Medical Society. To July 31, 1969, there has been expended from this fund for the purpose directed a sum of $1,525.00.

SCHOLARSHIPS

Awards

For the purpose of the record, the following scholarships in the sum of $500 each were granted by the Benevolent and Loan Fund Committee through mail vote between the period August 1, 1968 to July 1, 1969, which actions are reaffirmed:

Dixon, Patricia Anne (Tucson) — UofA
Douglas, Mel E. (Tucson) — UofA
Hendricks, Lynn Ann (Phoenix) — UofA
Kennedy, Timothy C. (Tucson)—Columbia College of Physicians and Surgeons
Kunkel, Joel W. (Tuscon) — UofA

Summary: 1968-69 (Fiscal Year) 12 Awards ($500.00 Each) $6,000.00.

Applications for Review

Following careful review and evaluation of each application in hand, the Committee approved and granted the following twenty-two (22) scholarships in the sum of $500 each, subject to the satisfactory completion of the file in several instances indicated below, and the registration of the applicants in approved medical schools or colleges of their choice, September next as first year medical students:

Applicant	Graduated
1. Beauchamp, Robert Frederick (Phoenix) To Attend: U of A College of Medicine	ASU
2. Breiman, Richard Spencer (Tucson) To Attend: U California S/F School of Medicine	U of A
3. Dahl, Steven I. (Mesa) To Attend: U of A College of Medicine	ASU
4. Federschneider, Jerome M. (Tucson) To Attend: U of A College of Medicine	U of A
5. Hooper, III Edward Young, Casa Grande) To Attend: U of A College of Medicine	U of A
6. Maciulla, Gregory James (Tucson) To Attend: U of A College of Medicine	U of A
7. Manning, Michael Rollin (Tucson) To Attend: U of A College of Medicine	U of A
8. McBride, Cris Dewaine (Tucson) To Attend: U of A College of Medicine	U of A
9. Nudo, Richard Anthony (Phoenix To Attend: U of A College of Medicine	ASU
10. Poliakoff, Raymond Marion (Tucson) To Attend: U Colorado School of Medicine	U of A
11. Qualls, Susan Patricia (Tucson) To Attend: U of A College of Medicine	U of A
12. Reineberg, Edward Jere (Eloy) To Attend: U of A College of Medicine	NAU
13. Roach, Mary Julia (Phoenix) To Attend: U of A College of Medicine	U of Michigan
14. Ruben, David Alan (Tucson) To Attend: U of A College of Medicine	Pomona College Claremont, Calif.
15. Schold, Jr., Stanley Clifford (Phoenix) To Attend: U of A College of Medicine	U of A
16. Soulliard, Mary Carol ,Tucson) To Attend: U of A College of Medicine	U of California L/A
17. Chick, Russell Paul (Scottsdale) To Attend: U of A College of Medicine NOTE: Subject to Completion of Reference	NAU
18. Freestone, Steven Wilford (Mesa) To Attend: U of A College of Medicine NOTE: Subject to Completion of Reference	ASU
19. Goggin, Daniel Anthony (Carefree) To Attend: U of Texas Medical Branch-Galveston	Abilene Christian College
20. Wasem, Donald Ben (Phoenix) To Attend: Albany College of Union University	Rutgers College New Brunswick, N.J.
21. Youngkin, Tyler (Phoenix) To Attend: U of A College of Medicine	NAU
22. Bedard, Charles Kent (Phoenix) To Attend: U of A College of Medicine NOTE: Subject to Satisfactory Completion of his Entire File, Application Having Been Just Recently Received.	ASU

Scholarship Fund Review

Considerable discussion ensued regarding the operation of the ArMA Scholarship Program. The Committee has been confronted with many problems relating to applicant requirements as prescribed by action of the House of Delegates in 1964 presently needing clarification; also, concern was expressed as to the financial status of the Fund in the light of declining interest earnings, the result of the current headquarters building project.

It was regularly moved and unanimously carried that there be referred to the Executive Committee of the Association for consideration the Scholarship Program of ArMA with a view possibly of introducing a resolution during the next Annual Meeting of the House of Delegates providing certain clarification for administration of the Program.

Referring to Resolution No. 14, adopted by the House of Delegates of this Association May 1, 1964, as amended, it is recommended that the second resolve be further amended to read:

> RESOLVED, that the Benevolent and Loan Fund Committee be directed to institute and proceed with a scholarship grant for any resident of Arizona who is attending as a freshman, his or her first years in an approved Class "A" medical school; this scholarship to amount to a Five Hundred Dollar scholarship from the Arizona Medical Association;

It was further directed that the Executive Committee be apprised of the financial problem confronting the Scholarship Program, and the potential program growth in the years ahead.

OTHER BUSINESS

Scholarship Applications

It was determined to review and consider applications for scholarships, funds being available, throughout the freshman first year of medical school, subject to concurrence therein by the Board of Directors and House of Delegates of this Association.

Arizona Residency

Determined for the present to accept "Arizona residency" as the legal Arizona residency certified by the applicant in his application. This is a major problem with our universities in determinng "out-of-state" residents for admission involving a tuition difference as against instate residents. The University of Arizona College of Medicine might be helpful at the time of registration of medical students to advise its determination as to residency.

MEETING ADJOURNED AT 12:35 P.M.

Edward Sattenspiel, M.D.
Secretary
by
Robert Carpenter
Executive Director

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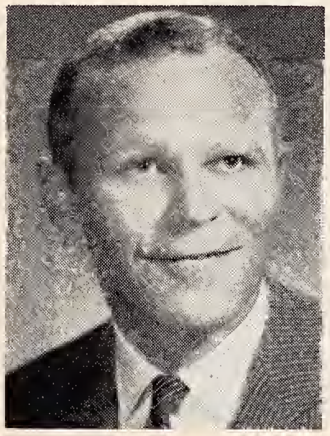
SEQUENTIAL PRIMARY TUMORS OF THE PANCREAS



Arthur R. Nelson, M.D.
Phoenix, Arizona

A belated report of two unusual tumors of the pancreas. Should this make us consider further Dr. Huebner's concept that malignancy is the end result of the interaction of four variables — susceptible genetic tissue, plus invasion by two viruses, plus trauma. (Further case studies are encouraged by the editor.)

The occurrence of sequential unrelated primary tumors in a single organ is indeed rare. The case reported herein has interest primarily because it represents a most unusual appearance of two decidedly rare tumors developing in an organ which is not noted for its compatability with the surgeon.

Mozan[1] collected the world literature on cystadenomas of the pancreas in 1951. At the time of his report there were only 49 definitive cases. Other authors have added a total of eight further reports in the American literature.[2, 3]

Cystadenoma of the pancreas presents clinically as a palpable mass. Associated dyspepsia, moderate pain and premature gastric satiation may be present. Diabetes occurs in only 14% (Mozan) and jaundice is only rarely a part of the clinical pattern.

The lesion is not malignant, but requires complete extirpation to prevent recurrence. There has been some argument as to whether the microscopic appearance of papillary projections within the musocal pattern of certain cystadenomas does not support the pathologic criteria of malignancy, but the clinical behavior of such tumors would certainly support its benignancy.

The secondary appearance of a distinctly different tumor of the pancreas following successful resection of the cystadenoma, leads to a host of philosophic queries as to organ potentials and consequences of surgical disturbance of an organ such as the pancreas. Suffice it to say that multiple pathologic consultations on the specimen removed at the second operation, confirm the presence of a neoplastic lesion typical of primary fibroma, again a rarity in the pancreas.

Case Report

L. S., a seventy-eight-year-old white female was admitted to hospital on 11-16-56 with the complaint of abdominal pain of three weeks duration. The pain was midepigastric, unassociated with position or state of satiation. There had been no emesis, melena, hematemesis or change in stooling pattern. Her past history was unremarkable save for a demonstrated duodenal ulcer seven years previously, which had responded to medical therapy.

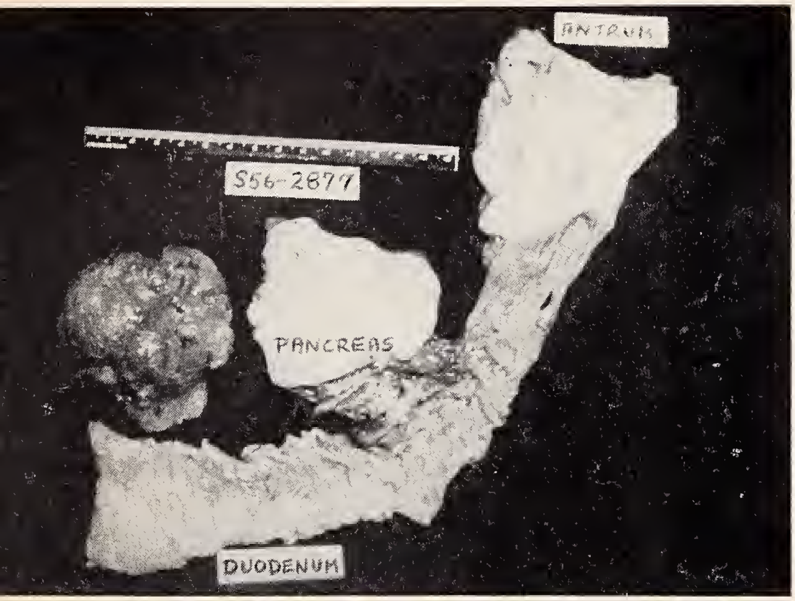


Figure 1
Gross surgical specimen of original pancreaticoduodectomy. The cystadenoma has been hemisected.

Physical examination was normal save for a palpable mass in the right hypochondrium measuring 8 x 10 cm, vertically movable, firm, and slightly tender. X-ray studies revealed moderate gastric stasis. The duodenal C-loop was not remarkable. Barium enema was normal save for diverticulosis. Laboratory studies were unrevealing. Of pertinence was the fact that there was no anemia, hypoproteinemia, or evidences of elevated blood sugar. Glucose tolerance test was normal.

Surgical exploration was carried out on 11-21-56. A pancreaticoduodenectomy[3, 4, 5] was completed for removal of a bulky cystic tumor of the head of the pancreas. (Fig. 1) The pathological report was that of benign cystadenoma of the pancreas measuring 8 x 7 x 4 cm with multicystic lesions of high cuboidal and low flattened epithelium. (Fig. 2) The margins of resection were clean, and there was normal acinar and islet structure with no evidence of obstructive change in the acini or ductal systems. There was scattered calcification. (Fig. 3)

The postoperative course was benign. There

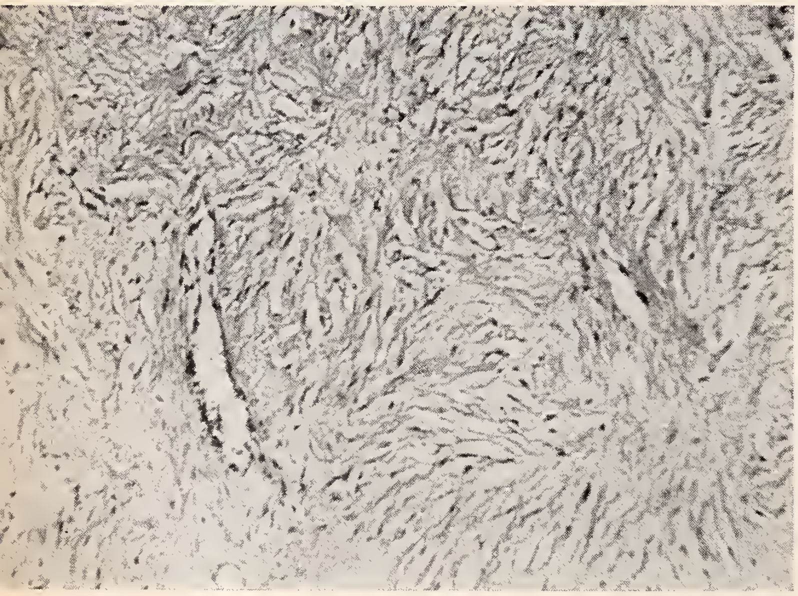


Figure 2
Microscopic detail of cystadenoma of pancreas, the original tumor.

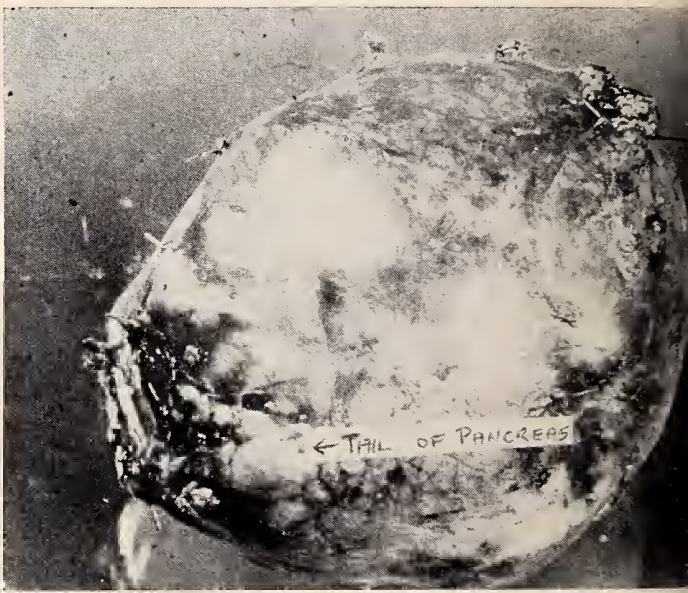


Figure 3
Gross appearance of the cystadenoma. Note its size as compared to the residual segment of normal pancreatic tail.

was mild pancreatic insufficiency with frothy stooling three to four times daily. A temporary diabetic curve ensued, but all symptoms were controlled with carbohydrate restriction and Pancreatin. The patient resumed normal activity and was discharged from hospital eleven days postoperatively.

During the ensuing two years, the patient was followed closely by the author. She maintained normal stooling with the use of Pancreatin tabs 2 tid and the occasional use of paregoric.

On 11-6-58 she was admitted as an emergency with a small bowel obstruction. Lysis of obstructing adhesions was carried out, and again her postoperative course was benign.

On March 18, 1959 she was again admitted with the complaint of having noted a "hard area" in her abdomen. She had sustained a four pound weight loss. There was no abdominal pain, change in stool habit, or other symptoms. Examination revealed a firm nodular mass in the left upper quadrant, movable, non-tender, and measuring about 6 x 8 cm.

Upper and lower intestinal X-rays were unremarkable save for the changes associated with the previous Whipple procedure. Hematocrit 40.5; hbg 12.5; wbc 5,000 with normal differential. Urine and blood studies were negative, with particular note of the absence of diabetes.

Exploration was completed on 3-27-59. A firm, grey-yellow, non-cystic tumor of the residual body and tail of the pancreas was resected, leaving about one inch of residual body adjacent to the previous area of implantation into the jejunum. (Fig. 4)

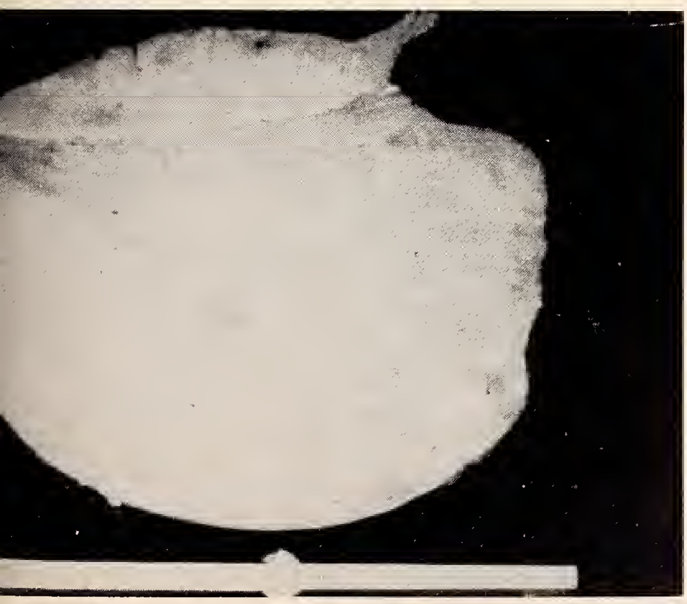


Figure 4
Gross section of the second primary tumor, a cellular pancreatic fibroma.

The pathologic examination is quoted: "The specimen is of extreme interest. The fibroma is markedly cellular, but we are reluctant to make a diagnosis of malignancy. The fibroma is much more cellular than the fibroustissue components of the previous cystadenoma removed three years ago. However, there is no evidence of active proliferation of the epithelial component at present." (AGF) (Fig. 5)

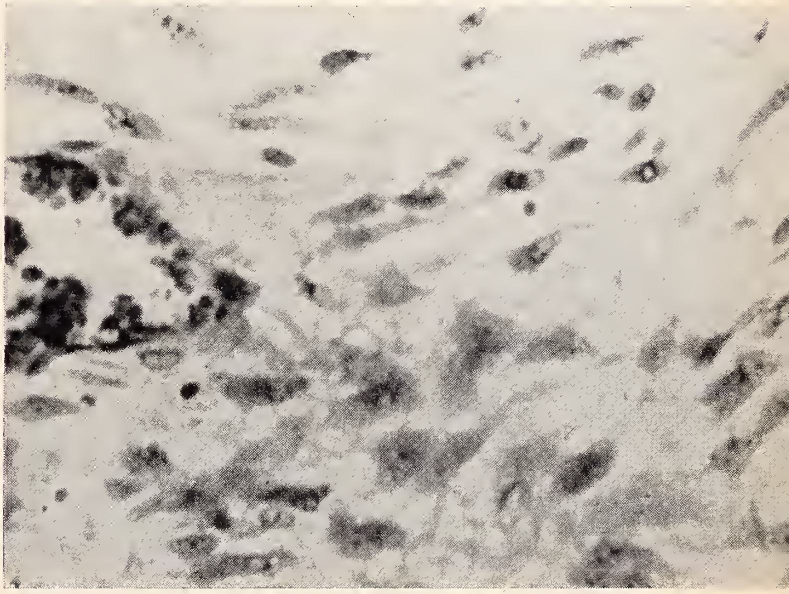


Figure 5
Microscopic detail of fibroma.

Again the patient recovered and was discharged home. Her steatorrheal stools were accentuated and required almost continuous use of antidiarrheal agents. However, she maintained good nutrition and was active in church work despite her advanced years.

The patient died of congestive heart failure, acute, on 8-23-59. Autopsy was not obtained.

Summary

Sequential primary tumors of the pancreas, the first a benign cystadenoma, followed in two years by the development of a cellular fibroma are described. Both lesions were successfully treated by surgical excision.

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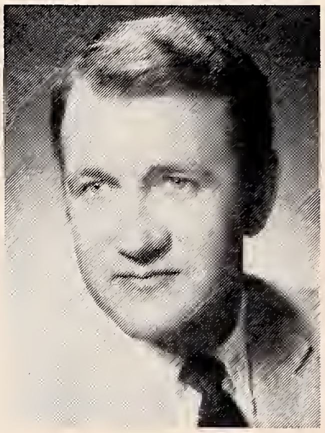
DERMATOPHYTES IN TUCSON, ARIZONA, 1967 AND 1968



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Synopsis-abstract

A survey was made of dermatophytosis of patients from private practice in Tucson, Arizona during 1967 and 1968. Classification of the organisms originally cultured on Sabouraud's medium plus antibiotics and Littman's ox gall agar was based on gross and microscopic morphology. Nutritional media were used to identify organisms that were not readily classified using morphology. The most frequently isolated fungal pathogen was *Trichophyton rubrum. Microsporum canis* was the prominent cause of tinea capitis and the second most frequently isolated pathogen for all dermatophytoses. No cases of tinea capitis caused by *M. audouinii* were found. A few isolations of *T. tonsurans* were made including one from a case of tinea capitis. Though *T. mentagrophytes* was the third most frequently isolated pathogen, the number of isolations was notably different for both years. The occurrence of *M. gypseum, Epidermophyton floccosum,* and *Malassezia furfur* was similar to other areas of the United States.

Only two surveys have been made of fungal, cutaneous diseases in the arid, southwestern United States. Lehmann and his associates[1] reported a survey of tinea capitis from private patients in San Antonio, Texas in 1950. Mullins[2] reported on a survey for tinea capitis of school children between the ages of 6 and 12 in Phoenix, Arizona in 1954. This is a report on dermatophytes from patients in private practice seen in Tucson, Arizona during 1967 and 1968.

Materials and Methods

Specimens collected in sterile, plastic petri dishes or non-sterile glassine envelopes were submitted by the dermatologists of the city and by the physicians at the Student Health Service at the University of Arizona. Direct microscopic examinations were made of these following treatment with potassium hydroxide and ink. The specimens were cultured at room temperature on two media: Sabouraud's dextrose agar plus cycloheximide and chloramphenicol, and Littman's ox gall agar (Difco Laboratories, Detroit, Mich.). To prevent drying of the media because of low relative humidity, large rubber bands were used to hold the glass petri dish halves together. All cultures were kept for three weeks before they were considered negative.

When fungal organisms were isolated, they were identified by their gross and microscopic morphology. In some instances, urea medium was used to differentiate *Trichophyton mentagrophytes* from *T. rubrum* when these isolates were not typical of the species.[3] Nutritional tests were also used to separate *T. mentagrophytes* from *T. tonsurans* when these organisms were not typical grossly or microscopically.[4] Nutritional tests were also used to identify *T. verrucosum.* Identification of the organism causing tinea versicolor, *Malassezia furfur,* was based on direct observation of the organism on skin scales. Yeast isolates were transferred to corn meal plus Tween 80 medium on slides.[5] Non-ascosporic organisms which produced mycelium or pseudo-mycelium with chlamydospores in abundance on this medium were identified as *Candida albicans.* The isolates not producing abundant chlomydospores were identified using fermentation and assimilation reactions.[5]

TABLE 1 - DERMATOPHYTOSIS IN TUCSON, ARIZONA, 1967

	DISEASE							
ORGANISM	Tinea Corporis	Tinea Capitis	Tinea Pedum	Tinea Cruris	Onycho-mycosis	Tinea Manuum	Tinea Versicolor	Totals of Infected Patients
M. canis[2]	20	15	1					34[4]
M. gypseum[3]	2							2
T. rubrum[1]	8		17	10	3	2		39[4]
T. mentagrophytes[1,2]			8		1			9
T. tonsurans[1]		1						1
E. floccosum[1]			2					2
M. furfur							8	8
C. albicans				3	2			5
TOTALS	30	16	28	13	6	2	8	100

1. Anthropophilic
2. Zoophilic
3. Geophilic
4. Patients with more than one infected site counted once.

Results

The results of the survey in 1967 are given in Table I, and the results of the survey in 1968 are given in Table II.

Comment

The predominance of *M. canis* as the cause of ringworm of the scalp in the arid cities of San Antonio, Phoenix and Tucson, is in contrast to the remainder of the cities of the U.S. *Microscopic canis* is zoophilic, and is generally spread from animals to man.[6] It is a natural parasite on cats and dogs. This organism is the most prominent cause of tinea capitis in Tucson. Lehmann, Pipkin and Ressmann[1] reported 53% of the cases

TABLE II - DERMATOPHYTOSIS IN TUCSON, ARIZONA, 1968

	DISEASE							
ORGANISM	Tinea Corporis	Tinea Capitis	Tinea Pedum	Tinea Cruris	Onycho-mycosis	Tinea Manuum	Tinea Versicolor	Totals of Infected Patients
M. canis[2]	17	9						26
M. gypseum[3]		2				1		3
T. rubrum[1]	3		18	3	4	3		29[4]
T. mentagrophytes[1,2]	1		22					23
T. tonsurans[1]	2							2
E. floccosum[1]	1		3	2				6
M. furfur							7	7
C. albicans				2	1			3
T. verrucosum[2]					1			1
TOTAL	24	11	43	7	6	4	7	100

1. Anthropophilic
2. Zoophilic
3. Geophilic
4. Patients with more than one infected site counted once.

of tinea capitis in San Antonio, Texas in 1946 to 1948 to be caused by *M. canis*. These cases were from private practice. In 1954 Mullins,[2] in a school survey of tinea capitis in Phoenix, reported 26 of a total of 32 cases of tinea capitis as caused by *M. canis*. This is approximately 81%. The percentage of tinea capitis caused by *M. canis* in the 1967 survey in Tucson was approximately 94% and approximately 82% in the 1968 survey. The dominant causal organism for tinea capitis in the U.S. is now *M. audouinii.*[7] As reported by Lewis et al,[8] *M. audouinii* replaced *M. canis* as the predominant cause of tinea capitis. *Microsporum audouinii* is an anthropophilic organism and is transmitted from man to man.[7] Lehmann and his co-workers[1] found 19 of 170 cases of tinea capitis to be caused by *M. audouinii* and Mullins 3 of 32.[2] No isolation of *M. audouinii* was made in the present Tucson surveys.

Other areas that have *M. canis* as the predominant cause of tinea capitis are Cuba, Puerto Rico, Denmark, Finland, France, Great Britain, Australia, New Zealand, Argentina, Chile, Uruguay and the Cape Verde Islands.[7] Since these areas are not all arid, a dry climate does not appear to be the factor for the predominance of *M. canis* as the cause of tinea capitis.

A proportionally larger number of pets in Tucson might be the cause for the higher incidence of dermatophytosis caused by *M. canis*. No statement with statistical validity can be made concerning this relationship because: the disease is a relatively rare event; the methods for determination of infection are not uniform nor completely efficient, and the cat populations are not known and cannot be inferred from the registered dog populations.

The rarity of *T. tonsurans* as the cause of dermatophytosis in Tucson was not expected. This anthropophilic organism is the predominant cause of tinea capitis in Mexico. During the last twenty years there has been increased incidence of *T. tonsurans* as the cause of tinea capitis in the U.S.[7] An eight-fold increase of infections by *T. tonsurans* from 1964 to 1966 was reported by Rosenthal and his co-workers[9] in New York City. In the San Antonio survey in 1946 to 1948, 18 of 170 cases of tinea capitis were caused by *T. tonsurans.*[1] In the Phoenix survey reported in 1954, 3 of 26 tinea capitis cases were caused by *T. tonsurans.*[2] The reason or reasons for the apparent low incidence of this organisms in Tucson is not known. The incidence of *T. rubrum* and *T. mentagrophytes* in the 1967 survey is the same as that reported for other areas of the U.S. The ratio of *T. rubrum* to *T. mentagrophytes* in the 1967 survey was 4:1; the same as that reported by Maskin et al.[10] Maskin and his associates reported a shift from *T. mentagrophytes* to *T. rubrum* as the etiological agent of dermatophytosis as the result of their investigation from 1935 to 1954. The ratio of the two etiological agents did not remain the same in the 1968 survey in Tucson. In that year the ratio of *T. rubrum* to *T. mentagrophytes* was approximately 4:3.

The incidence of *E. floccosum, M. gypseum* and *M. furfur* is similar to that in other cities in the U.S. The incidence of *C. albicans* is low. Since some of the skin scales were not placed on media immediately after the specimen was taken, but were stored for several weeks, these organisms may have died before plating.

The single isolation of *T. verrucosum* in the 1968 survey was from a patient who had formerly lived in the middle west. This organism is zoophilic[7] and has not been reported from Arizona before. It is assumed that the causal organism in this case was acquired before the patient moved to Arizona.

Acknowledgments

The assistance of the following physicians is gratefully acknowledged: Robert L. Andersen, Carl Z. Berry, Louis A. Brunsting, Sr., Richard F. Dahlen, Otis B. Miller, Richard C. Miller, Michael M. Schreiber and Seymour I. Shapiro.

Generic and Trade Names of Drugs

Cycloheximide — **Actidione**
Chloramphenicol — **Chloromycetin**

Work Sponsored

This research was supported by National Science Foundation Institutional Grants 5701-003-811as and 5401-098-003.

Indexing terms
Dermatophytosis
Trichophyton
Microsporum
Epidermophyton

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President's Page

"The condition of the medical care system which so badly serves the poor serves us badly too. In the immediate future all consumers will suffer the consequences of a badly organized, inadequately staffed, poorly distributed medical system."

"Our health is too important to leave to the doctors alone."

"Group practice (pre-paid with salaried physicians) is the only economical way to get efficient medical care."

We have all read and heard these and like statements for years, and tend to ignore them as the mutterings of some mal-contents or dedicated socialists.

Some of the things that make it hard to ignore some of our enemies is that the poor don't get adequate medical care. The cost of medical care now is almost prohibitive without insurance of some kind. The distribution of physicians between urban and rural areas and between specialists and general practitioners is uneven. An increasing number of our own members, many of our "friends" in local and state government and the present national administration which medicine worked hard to elect all feel that there are problems in the medical care system and something must be done about it.

The hardest problem for organized medicine is to convince its members that there are some deficiencies that should be corrected and to want to try to correct them. The old solution of waiting for the kooks to lose interest in medicine and attack somebody else, or to state that doctors know best and we will solve the problems or vote the straight Republican ticket will no longer suffice. Those of you who have read this far will notice that I have not given a solution to the delivery of health care. The main reason is that I do not have it right off hand, but I do think that medicine will be able to come up with a solution if we are convinced there is a problem. As we tell our obese or alcoholic patients, once you realize you have a problem, you are halfway to a solution. If I can solve half the problem by making you aware of it, surely you can solve the other half.

Richard O. Flynn, M.D.
President

Dean's Page

PERSONNEL: DEPARTMENT OF PSYCHIATRY

Early in the course of developing a new medical school one is forced to review the organizational strengths and weaknesses of the traditional medical schools and ask what should have representation in the new school's struture. Psychiatry is a particularly interesting discipline to consider in this vein because of its relationship to the broader field of behavioral science. Some medical schools have acknowledged this relationship by establishing departments of psychiatry and behavioral science; others, by making behavioral science or psychology a division of the department of psychiatry.

We believed that neither of these solutions was entirely adequate for the future. Instead, we took the position that behavioral science really consists of three entities: First there is the ecology of the physician, i.e. the circumstances and environment that surround him in his practice and which guide him toward actions appropriate to the conduct of his affairs. Ethics, medicine and public policy, cultural differences among patients, law, death and religion represent a sampling of that environment. We have established a Division of Social Perspectives in Medicine to treat these topics. Second, there is the ecology of the patient; that is, those factors that constitute the interaction between him and his environment and may largely determine his reaction to illness and its attendant circumstances. Third, there is psychiatry, a branch of medicine devoted to the management of a patient whose reactions to environmental circumstances are incompatible with a continued and rational pursuit of the experience of living. We plan to amalgamate the latter two types of behavioral science into our Department of Psychiatry.

But this doesn't tell the whole story. The academic orientation of psychiatry is usually dynamic, analytic or chemical, and our medical schools provide a wide representation of these orientations. In Arizona, we are taking the position that another element must now be added to the scene; more than that, it should be emphasized for the benefit of the students. The element is one of concern for the mental health of the people of the community as an expression of their reactions to the problems of contemporary society. This is a complicated problem and one in which we have very limited experience. Our Department of Psychiatry, especially in concert with the effort of our Department of Community Medicine, will try to further our knowledge and our competence in this area. To do this, we have intentionally identified, and attracted to our company, a leader in contemporary thinking relative to community mental health.

Dr. Alan Levenson was born in Boston, Massachusetts in 1935. He received his Bachelor's Degree at Harvard College in 1957, summa cum laude and was elected to membership in Phi Beta Kappa; he received his M.D. degree from Harvard Medical School in 1961 and in 1965 his Master's degree from the Harvard School of Public Health. Dr. Levenson interned at the University of Michigan and completed residency training in psychiatry at the Massachusetts Mental Health Center in Boston. He is certified in psychiatry by the American Board of Psychiatry and Neurology.

In 1965 Dr. Levenson joined the Community Mental Health Facilities Branch of the National Institutes of Mental Health as a staff psychiatrist. Subsequently, he advanced to the position of Director of the Division of Mental Health Service Programs of the NIMH. He has held faculty appointments at Harvard and at the Washington School of Psychiatry. He is a fellow of the American Psychiatric Association, the American Public Health Association, the American Medical Association and the Group for the Advancement of Psychiatry. Dr. Levenson has served as a member of the Advisory Committee on Mental Health for Montgomery County, Maryland and is a member of the Board of Directors of the Montgomery County Mental Health Association. He is the author of numerous publications in the general field of community mental health.

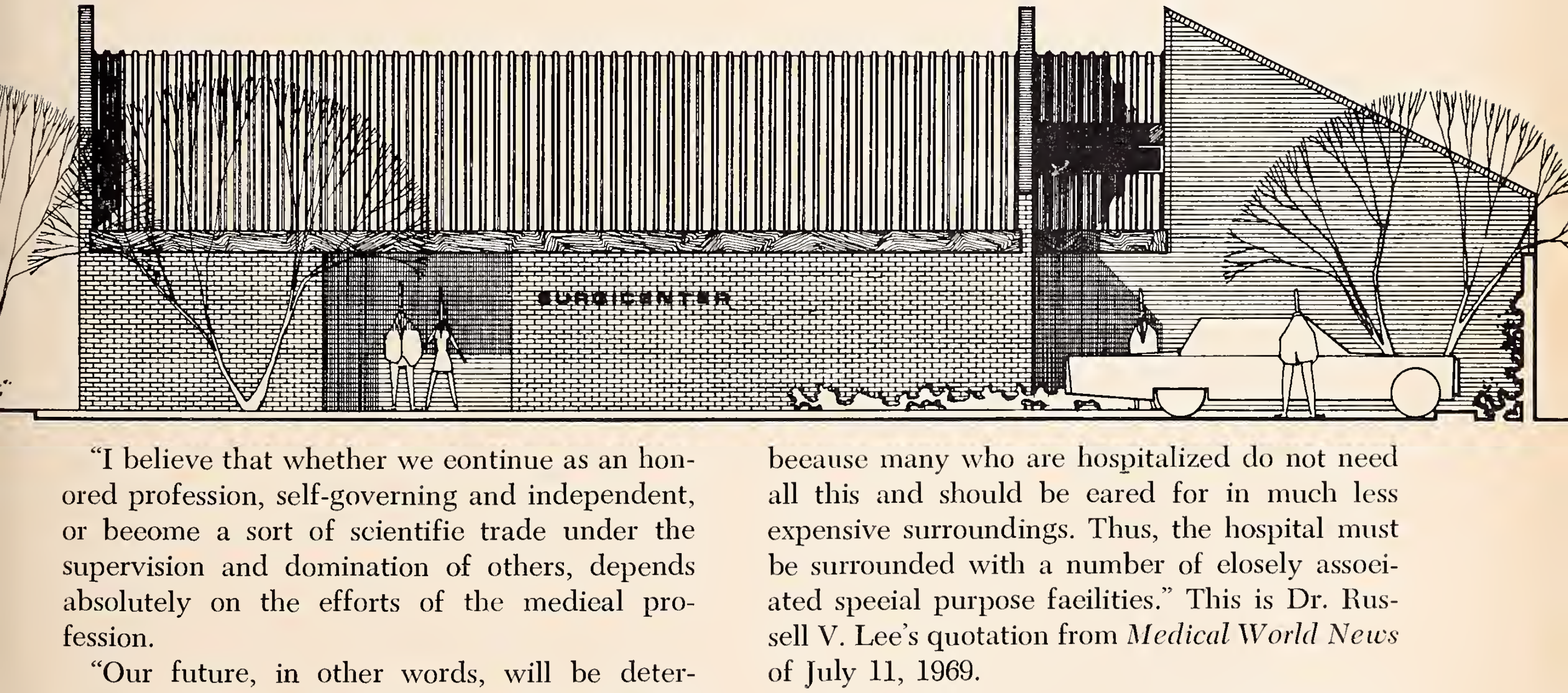
As noted above, we feel that Dr. Levenson represents tomorrow's look in the field of psychiatry and we welcome him warmly into the College of Medicine as Professor and head of our Department of Psychiatry.

Monte DuVal

THE SURGICENTER

AN INNOVATION IN THE DELIVERY AND COST OF MEDICAL CARE

JOHN L. FORD, M.D. **WALLACE A. REED, M.D.**



"I believe that whether we continue as an honored profession, self-governing and independent, or become a sort of scientific trade under the supervision and domination of others, depends absolutely on the efforts of the medical profession.

"Our future, in other words, will be determined by how fast and how well the medical profession recognizes its responsibilities, and how fast and how well it discharges these responsibilities." So was AMA Past-President Dr. James J. Appel quoted in the June 1969 issue of *Massachusetts Physician.*

"The Modern hospital is rapidly becoming an intensive care unit with all the fantastically expensive equipment and procedures that are required. It costs too much; it costs too much because many who are hospitalized do not need all this and should be cared for in much less expensive surroundings. Thus, the hospital must be surrounded with a number of closely associated special purpose facilities." This is Dr. Russell V. Lee's quotation from *Medical World News* of July 11, 1969.

The Surgicenter is one such special purpose facility, an effort by members of the medical profession, the prime objective of which is to discharge well some of our "responsibilities."

The building to house the Surgicenter is under construction at 1040 East McDowell Road, Phoenix, in handy proximity to Good Samaritan Hospital. The heart of the facility will be the four operating rooms and the large recovery room. Appropriate ancillary equipment and rooms are included in 5240 square feet encompassed in the building. (Figure 1)

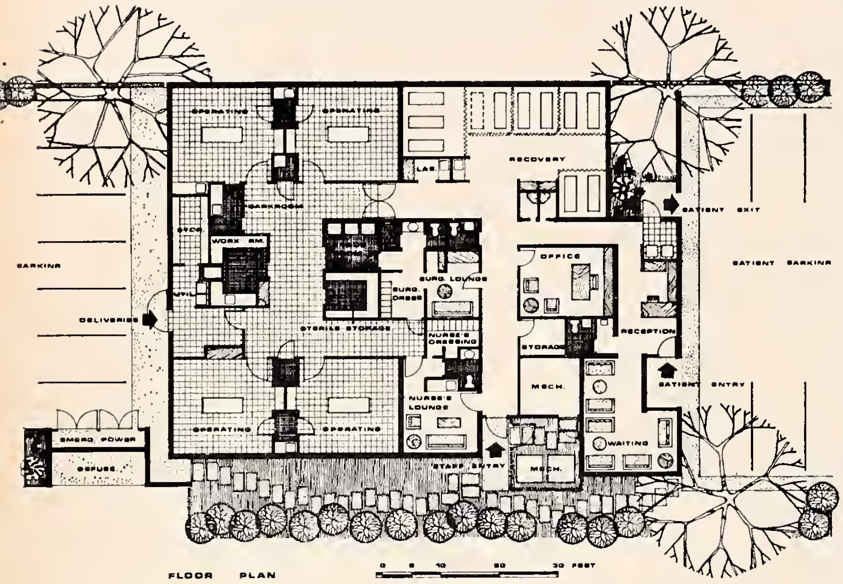


Figure 1

Among the responsibilities which the authors hope to discharge with the concept of the Surgicenter are these:

- To make the "ambulatory patient" a matter of greater concern.
- To streamline the delivery of his medical services.
- To reduce the cost of his care.
- To work for a broadening of his insurance coverage.

Two facilities similar to the Surgicenter are already operational in Los Angeles, California and in Washington, D.C. Each is under the jurisdiction of hospitals maintained by medical schools. In each instance the expense of the delivered care, compared with inpatient cost has been appreciably reduced without sacrifice of quality.[1, 2]

Dr. William Dornette, an authority in the field of health planning, has stated that a Surgicenter type facility can operate independently of a hospital, and the authors subscribe to this view:

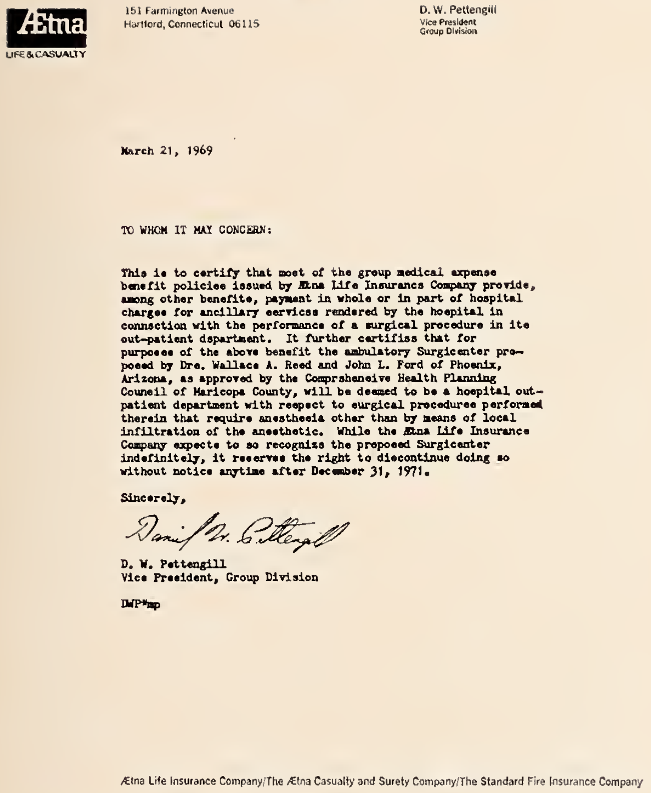
"One facility about which little has been written is the outpatient service offering general anesthesia for minor surgical procedures. Such a facility, properly designed, staffed, and operated, has several advantages. A significant patient load is removed from the inpatient bed and operating facilities. There is a distinct savings in the cost to the patient or to the patient's hospitalization insurance carrier. The operation of one such facility (at UCLA) as part of a hospital's outpatient department, and the advantages accrued to such operation, are well documented. *But a safe and efficient facility for performance of general anesthesia and minor surgical procedures need not be affiliated either administratively or geographically with a hospital.*"[3]
[Emphasis added]

While the concept as suggested by Dr. Dornette is simple in principle, infusing it with life is another matter altogether. There has been no precedent to follow, and many obstacles presented themselves as the project was developed. One thing that was certainly obvious from the outset was that we needed approval from major insurance carriers. Also, we wanted to establish an effective means for quality control. As it turned out, our interest in achieving quality control proved to be the key to a workable formula: We gained the cooperation and approval of the Comprehensive Health Planning Council of Maricopa County; and with their help, developed an "Agreement" which outlines a method for maintaining high standards. Chief among the stipulations is that a Medical Audit Committee consisting of at least three physicians "will regularly review the medical and surgical procedures and practices employed in our facility with the power to recommend and to enforce standards which are on a par with those employed in an accredited community general hospital in the metropolitan-Phoenix area and who will also recommend practices designed to avoid overutilization of our facility. These physicians will receive a nominal fee for serving on this Medical Audit Team and will accept appointment to such team in writing, wherein they will state that they have no economic or other vested interest in the facility. Persons selected for this Medical Audit Team shall receive prior endorsement from the appropriate local professional-specialty or general practice society or in its absence the Board of Directors of the Maricopa County Medical Society."[4]

We used the Agreement worked out with the Comprehensive Health Planning Council of Maricopa County as the basis for our discussions with various insurance carriers. We received official recognition from a major carrier in April, as is evident from Figure 2.

Several other carriers have made similar changes in their contracts, and many have indicated their willingness to cooperate when the Surgicenter opens. CHAMPUS (Military Medicare) has endorsed the concept wholeheartedly

Figure 2



Ætna
LIFE & CASUALTY

151 Farmington Avenue
Hartford, Connecticut 06115

D. W. Pettengill
Vice President
Group Division

March 21, 1969

TO WHOM IT MAY CONCERN:

This is to certify that most of the group medical expense benefit policies issued by Ætna Life Insurance Company provide, among other benefits, payment in whole or in part of hospital charges for ancillary services rendered by the hospital in connection with the performance of a surgical procedure in its out-patient department. It further certifies that for purposes of the above benefit the ambulatory Surgicenter proposed by Drs. Wallace A. Reed and John L. Ford of Phoenix, Arizona, as approved by the Comprehensive Health Planning Council of Maricopa County, will be deemed to be a hospital out-patient department with respect to surgical procedures performed therein that require anesthesia other than by means of local infiltration of the anesthetic. While the Ætna Life Insurance Company expects to so recognize the proposed Surgicenter indefinitely, it reserves the right to discontinue doing so without notice anytime after December 31, 1971.

Sincerely,

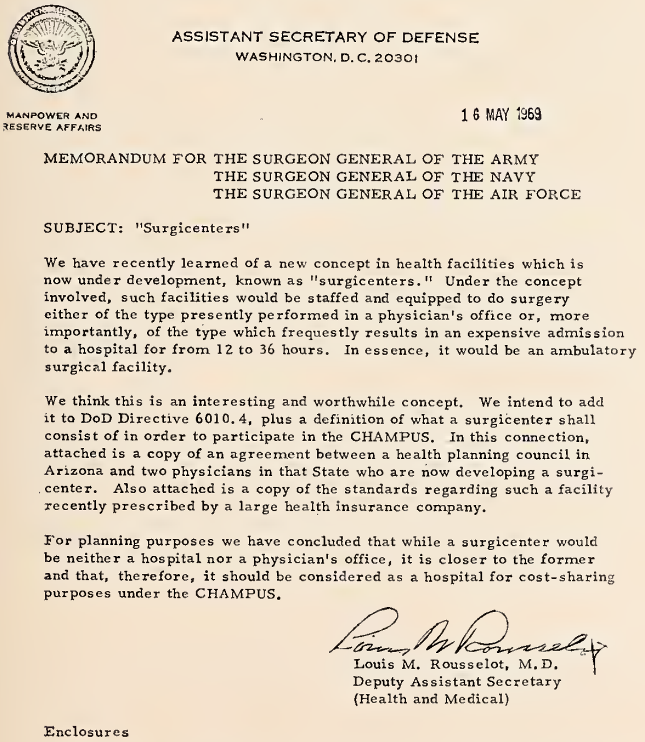
Daniel W. Pettengill

D. W. Pettengill
Vice President, Group Division

DWP*mp

Ætna Life Insurance Company/The Ætna Casualty and Surety Company/The Standard Fire Insurance Company

as evidenced by a Memorandum dated 16 May 1969, the full text of which is shown below:



ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D. C. 20301

MANPOWER AND
RESERVE AFFAIRS

16 MAY 1969

MEMORANDUM FOR THE SURGEON GENERAL OF THE ARMY
THE SURGEON GENERAL OF THE NAVY
THE SURGEON GENERAL OF THE AIR FORCE

SUBJECT: "Surgicenters"

We have recently learned of a new concept in health facilities which is now under development, known as "surgicenters." Under the concept involved, such facilities would be staffed and equipped to do surgery either of the type presently performed in a physician's office or, more importantly, of the type which frequently results in an expensive admission to a hospital for from 12 to 36 hours. In essence, it would be an ambulatory surgical facility.

We think this is an interesting and worthwhile concept. We intend to add it to DoD Directive 6010.4, plus a definition of what a surgicenter shall consist of in order to participate in the CHAMPUS. In this connection, attached is a copy of an agreement between a health planning council in Arizona and two physicians in that State who are now developing a surgicenter. Also attached is a copy of the standards regarding such a facility recently prescribed by a large health insurance company.

For planning purposes we have concluded that while a surgicenter would be neither a hospital nor a physician's office, it is closer to the former and that, therefore, it should be considered as a hospital for cost-sharing purposes under the CHAMPUS.

Louis M. Rousselot

Louis M. Rousselot, M.D.
Deputy Assistant Secretary
(Health and Medical)

Enclosures

As of this writing, we have not met with the Arizona Blue Cross Board of Directors, which has set a date in September as the time to review the Surgicenter concept. However, it is worthy of note that in the State of Arizona, Blue Cross is the fiscal agent for CHAMPUS, which has approved our proposal. The authors are encouraged to believe that Blue Cross will also endorse the idea, since there are already signs pointing in that direction. One such sign is that in New York, Blue Cross has asked the State Insurance Department to approve a change in benefits in certain policies to encourage use of outpatient facilities and discourage unnecessary use of inpatient beds. In addition, Mr. Walter J. McNerney, President of the National Blue Cross Plans, has stated in reference to methods of delivery of health care that, ". . . all laws standing in the way of experimentation should be struck down."[5] He has recognized that, ". . . we in this country are going to stay with a pluralistic system of providing and financing medical care —a system involving both Government and private operations," and we should ". . . exploit fully the assets of the private sector."[6]

At its meeting in September, the Arizona Blue Cross Board will consider these features which make the Surgicenter unique:

1. It is more than a doctors' office, yet less than a hospital; and is independently operated. (However, transfer agreements with two major hospitals provide for the patient's continued care if indicated.)
2. It has been designed "from the ground up" to suit the particular requirements of the come-and-go patient, a fact which helps to keep the cost of care at a minimum.
3. With the exception of the physicians' fees, a single, all-inclusive charge will be made for each procedure. While the charge for an infant herniorrhaphy will be greater than for a cystoscopy, there will be a pre-set charge for each. This means that each patient, each surgeon, and each insurance carrier will know in advance of the operation exactly what the cost for a given procedure will be.

Since the Surgicenter is not a hospital in the legal sense, no licensure by the State Department of Health is required. Nevertheless, the authors asked State Health Department officials to review the project, with the result that several excellent suggestions made by them were incorporated into the final plans. The Acting Commissioner, Henry D. Smith, M.D., wrote under date of May 23, 1969, as follows:

> ". . . we feel your facility is both structurally and functionally sound. It is indeed refresh-

ing to see new approaches being made in the delivery of health care services."

The above instance is in keeping with the policy of the authors to inform all interested parties of our plans, and invite their questions and comments.

Thus, early in the year, we discussed our ideas with three different hospital administrators, all of whom assured us we can count on their cooperation. On February 11, the Board of Directors of the Maricopa County Medical Society were apprised of our plans. Dwight Wilbur, M.D., when President of the American Medical Association, wrote that he was interested in reading about the plan and wished us success in implementing it. In a recent communication with Mr. Chris N. Theodore, Director of the A.M.A.'s Division of Health Services, we provided him with pertinent information; and a copy of his letter with enclosures was sent to Arizona's A.M.A. delegation.

We have welcomed suggestions from our colleagues, and have discussed with them in detail the ways in which this facility can serve the needs of surgeons and their patients. Their enthusiastic response indicates clearly that, contrary to current popular opinion, doctors *are* interested in the cost of medical care. Nurses with whom we have discussed the matter have shown a similar interest; and those who are to help us launch the project have spent many hours on the plans and in the selection of the instruments to be made available to surgeons using the facility.

Gerald D. Dorman, M.D., currently President of the American Medical Association, wrote in JAMA of August 11: ". . . we must foster innovation in delivery of health care, we must improve our efficiency, and we must develop our highest possible level of ethics and self-discipline . . . we need local answers to local problems in each area."

We submit the concept of the Surgicenter as a step in the direction pointed out by Dr. Dorman; and emphasize that it is being constructed and will be maintained without cost to the taxpayer, local, state, or federal.

The Surgicenter concept certainly appears to fit into the "basic philosophy" of the current administration, judging from remarks attributed to former HEW Secretary John Gardner. Mr. Gardner is quoted by the *American Medical News* (August 18, 1969) as stating we need more fruitful relationships between the public and private sectors. Forces now at work tend, says Mr. Gardner, "to squeeze out pluralism, and to move us toward one comprehensively articulated system of power. We must work against that trend . . . As I contemplate that trend, I find myself treasuring every remaining bit of pluralism, everything that stands between us and the one all-embracing system . . ." Herbert Marcuse favors a more "directed" society, Gardner said. "In doing so, he makes the assumption made by all who fall into authoritarian doctrines — that, in the 'directed' society he envisages, people who share his values will be calling the tune. So thought the businessmen who supported Hitler."

While the primary function of the Surgicenter is to serve the particular needs of the ambulatory patient and his surgeon, it is not intended to be used as an emergency-care center. Experiences elsewhere indicate that the real emergency belongs in the hospital environment. Nevertheless, it is worth noting that the facility would be readily available and immediately useful to the community in time of a major disaster of any kind.

In summary, the Surgicenter is a response from the private sector to the many urgent appeals from the government, labor, industry, and the medical profession to streamline the delivery of medical care and reduce its cost. It is designed to provide quality surgical care to the patient whose operation is too demanding for the doctor's office, yet not of such proportion as to require hospitalization. Numerous advances in surgical technics, together with new local and general anesthetic agents, have been utilized successfully at teaching hospitals to treat the come-and-go patient. The authors intend to demonstrate with the Surgicenter that an independently-operated facility can function as successfully with even greater savings to the patient while maintaining high standards of care.

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RICHARD WILLEY, Ph.D.
Director, Division of
Social Perspectives
in Medicine

"THE OBJECTIVE OF THE DIVISION IS TO PROMOTE UNDERSTANDING OF THE IMPLICATIONS OF ADVANCES IN THE BIOLOGICAL SCIENCES AND THE PRACTICE OF MEDICINE, FOR HUMAN WELFARE, VALUES AND DIGNITY."

A NEW APPROACH IN EDUCATING PHYSICIANS

If it is true that an era of unprecedented change is upon us, and the indications are that it is, then the ability to understand and cope with change must logically take its place among the imbued skills of the emerging generation of new physicians. This is all the more important today, because the medical-sociological changes taking place now are not gradual and isolated; they are rapid, and are permeating all segments of the national community. These changes are affecting medicine in a variety of ways because, as Dr. Iago Galdston has said, ". . . it has become abundantly clear that medicine is more intimately bound to the destinies of state and community than is or has been recognized and acknowledged."

The Division of Social Perspectives in Medicine at the University of Arizona College of Medicine is in part a practicum for exploring the implications of some of these changes. It is a comparatively new approach to an old requirement that our institutions of higher learning be sentinels and critical evaluators of what is new and relevant. The Division approaches its mission by bringing faculty and students together for concentrated interface with ideas which have not traditionally been found in a medical curriculum. The bringing together is being done through a series of day-long "Cultural Horizons of Medicine" seminars, and the ideas explored range from the ethics of experimentation on man to controversial health legislation; the goals of medicine regarding life and death, to the control of human behavior.

The objective of the Division of Social Perspectives in Medicine is to promote among both faculty and students consideration and understanding of the implications of advances in the biological sciences and the practice of medicine, for human welfare, values, and dignity.

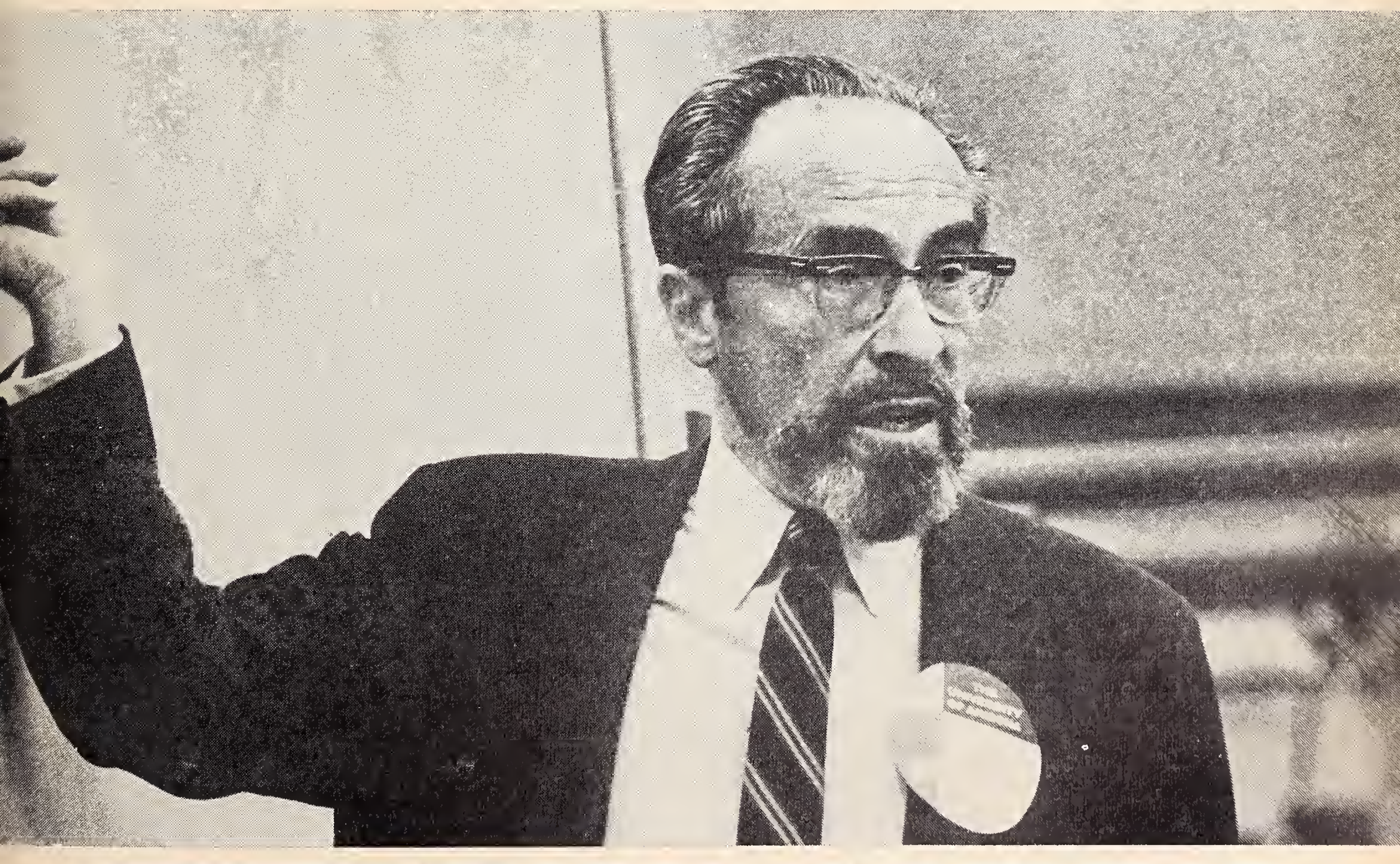
By so doing, the Division hopes to instill in the future physician an understanding of how the practice of medicine influences, and in turn is influenced by, other professions or segments of society and how the impact of political and social movement affects patterns of medical care. The program, in addition, urges the student to clarify his own moral and ethical values which relate to the new problems posed by medical research developments. To better understand the intent of the seminars it is helpful to examine one; in this case the seminar on "The Control of Brain, Mind, and Behavior."

Not so long ago, the idea of controlling the mind with push buttons, electrodes, and chemicals was thought to be a proper subject primarily for science fiction. Current research indicates, however, the modification of human behavior of one sort or another has already raised serious professional, social, and ethical questions. To discuss the state-of-the-art and some of the complex issues in this volatile field, two eminent researchers participated with students and faculty from the University of Arizona College of Medicine, College of Law, the departments of Sociology, Anthropology, Psychology, and Physics in a seminar on the subject.

The purpose of the seminar was to explore

"OUR ABILITY TO MANIPULATE BEHAVIOR BY THE USE OF DRUGS OR ELECTRICAL STIMULATION OF THE BRAIN IS LIMITED." — DR. KETY several basic questions. Among these were: 1) What kinds of control of human behavior are now possible by means of drugs? 2) Are these methods for manipulating human behavior fundamentally any different from the manipulation accomplished by traditional education and mass media? 3) Given these new techniques, what results do we want to achieve? 4) Who should have the responsibility for making the decisions needed and using the tools available?

Dr. Seymour Kety, Professor of Psychiatry at Harvard and past Scientific Director of both the National Institute of Mental Health and the National Institute of Neurological Diseases and Blindness, advised the audience that while we have made significant strides in developing tools for behavior modification, these developments are and should be limited. He said that "Our ability to manipulate behavior by the use of drugs or electrical stimulation of the brain is



"BY BETTER DEVELOPED PSYCHOLOGICAL, BEHAVIORAL AND OTHER TESTS WE WILL BE ABLE TO MAKE DIFFERENTIAL DIAGNOSES FOR PEOPLE CONCERNING THEIR LATENT INTELLECTUAL AND CREATIVE POTENTIAL." — DR. KRECH *limited,* first by the state-of-the-art; secondly by the relative ineffectiveness of these techniques as compared with more 'traditional' means of enforcing behavior along prescribed channels, and most importantly, by the inappropriateness of achieving socially useful behavior by the use of drugs."

Dr. Kety proposed that "socially useful" behavior could best be achieved by upgrading the quality of education and information to which society is exposed. He advocated concentrating on improving "traditional means of enforcing behavior" by improving our laws, our governmental structure, and our methods of handling those who deviate from society's parameters. Drugs, he felt, were justifiable perhaps only in an effort to ameliorate unusual behavior caused by biological defects, by disease processes or in some types of criminal behavior.

At mid-morning, Dr. David Krech, Professor of Psychology at the University of California at Berkeley and the second major speaker at the seminar, arose and stated that "My assignment, I understand, is to react vigorously to Dr. Kety — which I will proceed to do." He explained that he takes a much more apprehensive view of our future ability to alter the behavior of our fellow men. He picturesquely characterized the differences between Dr. Kety's view and his own: "Dr. Kety is rather pessimistic about the possibility of future research developments giving us effective control over human behavior and therefore is optimistic about society's ability to cope with these developments. I am much more optimistic about the likelihood of research giving us increased control over human behavior, and I am therefore more pessimistic about the ability of our society to cope with such developments." Dr. Krech explained that his pessimism was based on society's sluggishness in perceiving the implications of already existing laboratory research on behavior. He feels that the social control of deliberate efforts to influence the intellectual or emotional functioning of whole population groups through, for example, chemical additives to food, is made immensely more complicated by the fact that very constructive, as well as destructive, effects may be possible.

Pressed for his long-range view, Dr. Krech continued: "My view into the dim future is this. By better developed psychological, behavioral, and other tests we will be able to make differential diagnoses for people concerning their latent intellectual and creative potential. We may then very well be able to find specific educational and pharmacological treatments which will facilitate their specific abilities. And so, we will conceivably be able to 'build' good artists, good musicians, or good physicists."

Who will administer these drugs? Who will decide which segments of the population will be selected? According to Dr. Kresh, "Of one thing I am absolutely certain; the doctor cannot be the one to decide that. This is the kind of social policy that cannot be scratched out on the prescription pad of a practicing physician."

What about the ethical problems associated with the use of such drugs? According to Dr. Krech, "There have been many suggestions, and some of them go against the grain of everyone here, mine included. One is, that certain kinds of research not be done. Another is that a decision be made ahead of time by those who grant money as to what is, and is not, *fundable* research. Another device is the one we are engaging in today; open discussion of both the scientific facts and the social implications of the facts. It's an exciting problem. It concerns all of us."

The session devoted to control of the human mind resembled other programs of the Division of Social Perspectives in Medicine in at least two ways: 1) the topic was controversial and 2) the audience was not passive. The principal speakers were part of what was truly a day-long exercise in inquiry. The reaction which they stimulated included incisive questioning of their views, dissection of the topic in spirited group sessions, and floor debate among participants. The fact that the attendees were an admixture of diverse disciplines contributed even more to an overall atmosphere of intellectual expansion. It was the first time that many of those present had ever thought about the subject of behavior control, and regardless of their views either before or after the seminar, the significant thing was that they grappled with the subject and turned it over in their minds. I believe it is not important that the seminars impart blocks of specific factual information; what *is* important is that they stimulate tomorrow's doctor to think critically and thoughtfully about issues outside the laboratory and that they excite him to see new relations and new meaning among the many facets of contemporary life with which he is destined to deal.

IMPRESSIONS OF THE 118TH ANNUAL AMA CONVENTION

DANIEL T. CLOUD, M.D.

The 118th Annual AMA Convention zoomed into orbit on July 13, 1969. On that hot, sultry Sunday afternoon in New York City, the opening session of the 242 member House of Delegates was gaveled to order in the Imperial Ballroom of the great Americana Hotel by Speaker of the House, Dr. Walter C. Bornemeier.

It turned out to be a remarkable afternoon. After the customary prelusions, the United States Marine Drum and Bugle Corps was given the stage. They marched smartly out to a muffled drum beat, thirty-four elegant, clean-cut young men with polished silver trumpets tucked under their arms. Many had medals pinned on their neat crimson tunics. A few wore the Purple Heart.

On command they snapped the horns hard to their lips and thrilled the House and crowded gallery with a magnificent "Pageant of Flags." As the music of yesteryears filled the ballroom, The Red Cross of St. George, The Liberty Tree, The Grand Union Flag, The Stars and Stripes and all the legendary flags that trace our country's history were paraded splendidly across the stage.

You could see moist eyes in the audience. Most members of the House have served their country; some have shed blood for it; a few have given sons. All were keenly proud of this moment.

Then, when the last Marine had marched off to a thunderous, standing ovation, chaos erupted. A mob of perhaps seventy-five rather dirty young men and women, some wearing rumpled white clinical coats and carrying bits of medical paraphernalia, burst from the depths of the huge room, stomped forward with clatter and confusion and commandeered the podium and the Speaker's microphone. Trailing them were a pack of hungry news photographers. Television floodlights in the balconies glared over the scene like parachute flares.

For some twenty minutes they held the stage. One young doctor shouted scurrilities into the microphone and ceremoniously burned his AMA membership card. The other folks trooped around in circles chanting, "Hip, Hip, Hippocrates! Up with service, down with fees!"

And they carried big painted signs: "The American Medical Association — The American Murder Association." "Free Care For All." "Smash Fee For Service."

From the House there were shouts of: "Get a haircut." "Call in the Marines." A couple of ashtrays were lobbed into the swarm. But most of the Delegates watched with obvious boredom, or adjourned to the restrooms.

Finally the demonstrators milled out, still chanting and probably chapfallen that at least a couple of heads had not gotten busted. Their protest had crumbled pitifully. Its import was obscured by offensiveness. But they did chip the surface.

In the wake of this hurly-burly, the House braced for traditional oratory. Dr. Dwight L. Wilbur, the retiring AMA President, keynoted the convention. He spoke convincingly of embroidering our clinical sense with social sense and common sense. He urged voluntary health insurance for all and development of community health centers.

". . . we are practicing medicine in a goldfish bowl . . .," Dr. Wilbur rumbled. "Too often . . . we have let events and others control our destiny. . . . we must avoid cumbersome review mechanisms . . . by those not qualified. . . . must temper our clinical sense with a social sense. . . . must avoid the accusation that the AMA speaks to itself and not to . . . the public. . . . 20 to 40 million people are not getting the full benefits of what modern medicine and the physician have to offer. . . . health and medicine are not matters just for physicians and patients. They are matters of total public concern."

Next Dr. Roger O. Egeberg, the new HEW Assistant Secretary for Health and Scientific Affairs, was introduced to the House. Tall, soft-spoken and fatherly, he was plainly concerned about the rising costs of medical care and the urgent need of delivering care to those of our people who don't have it. He said, " . . . as a group, we must look around. . . . the poor live utterly differently from us. . . . we have created a distribution of medical care in a way that suits us and the middle class. . . . we've got to find new ways of distributing medical care. . . . we have come to a crisis. We have to solve it."

Thus the first session ended. The Marines regaled us, the demonstrators whooped, "murderers!" and the speakers unbosomed the great imparity in our national health care system.

The next day was less melodramatic. In the afternoon Vice President Spiro T. Agnew had some welcome pleasant words for the Delegates. He joked about "the Knowles affair" and cast Senator Dirksen in the role of "Secretary of Health, Education and Welfare — *ex officio.*" Vice President Agnew stated flatly that the AMA had been wrongfully charged with responsibility for the affair.

The Vice President went on to speak about the national problem of environmental pollution. He was impressive, not so much for his words or the bevy of burly, unsmiling Secret Service men that ushered him in and out of the ballroom, but because he projected warmth and sincerity.

On Wednesday evening a bouncy New Yorker, Dr. Gerald D. Dorman, was sworn in as the AMA's 124th President. In his inaugural address Dr. Dorman discussed the continually advancing health care system in America, methods of increasing respect for our medical leadership and recognition for our professional contributions, and the need to improve the functions of the medical profession.

Incidentally, the demonstrators tried to crash the inaugural ceremony and grab some prime television time, but they were quashed with the help of the New York Police Department. The House was in no mood for more foofooraw.

On the closing day of the convention, Dr. Dorman reported to the House. He probed many of the problems that now face medicine: quality of medical care, physicians who cheat, health care for the poor, voluntary health insurance, sex education, maternal and child health care, methods of delivering health care. And he hammered on the critical need to increase incentives for both the health profession and the public.

But with all the speeches, the demonstrations, and the incredible bovinity of the Americana restaurants, the House of Delegates managed to do business. And it was a great deal of business. There were 196 items considered, 59 reports and 137 resolutions, more than at any previous meeting.

Of the reports, 30 were adopted, 1 was adopted and referred, 5 were amended and adopted, 17 were approved, 2 were accepted for information, and 4 required no action.

Of the resolutions, 17 were adopted, 28 were adopted as amended, or a substitute was adopted, 30 were referred with or without amendment, 44 were combined with other resolutions before action was taken, 1 was partially adopted and partially referred, 15 were rejected, and 2 were withdrawn.

A significant report from the Board of Trustees Committee on Health Care For the Poor was adopted. This reiterated our strong commitment to expand nationwide programs to improve the health of the poor and stated that, "The same quality of medical care should be accessible to all people." Dynamic action in this field was given top priority in the AMA.

The agonizing problem of professional liability was ventilated exhaustively. It was determined that:

1. We seek the enactment of appropriate state legislation to provide more efficient and equitable determination of malpractice claims and litigation.
2. We attempt to develop pilot programs which will help provide scheduled benefits for persons injured as a consequence of medical accidents, irrespective of fault.
3. We establish workshops on malpractice insurance problems.
4. It is not feasible for the AMA to establish a nationwide professional liability program.

After a forty-five minute debate, the AMA bylaws were amended to permit membership for osteopaths who are accepted for membership in state medical associations.

The House, visibly concerned with the painful struggles of Medicaid, pledged a major action program to reduce Medicaid costs.

The twenty-three Scientific Sections of the AMA were given increased voice and responsibility in AMA activities.

The House approved a report that a physicians' relicensure program should not be considered at this time, but that peer evaluation be continuelly utilized and improved.

The House stated that the primary responsibility for family life education is in the home, and supported voluntary family life and sex education programs at appropriate grade levels. Guidelines for these programs were approved.

The rising cost of medical care was given top priority, and the House called for doctors to play a signifcant and responsible role in organized efforts to control health care expenditures.

The peer review concept was adopted as the most meaningful method for creating a public awareness of medicine's efforts to assure high quality of health services at a reasonable cost.

The House resolved to encourage the development of prepayment medical insurance programs utilizing the usual, customary or reasonable fee concept, and to urge the passage of legislation that would provide a program of income tax credits for financing prepaid health care.

The House reaffirmed its position (1) that it is a basic right of every citizen to have available to him adequate health care; (2) that it is a basic right of every citizen to have a free choice of physician and institution in the obtaining of medical care; and (3) that the medical profession, using all means at its disposal, should endeavor to make good medical care available to each person.

In a change of policy regarding federal loans to medical students, the House called for an increase in financial support of medical schools by the federal government to permit a major increase in enrollment of medical students and the production of physicians. This change was made because current high interest rates and restrictive supply of money for personal loans are making it difficult for students to obtain loans from the private sector.

The House reviewed the ethics of clinical laboratories and determined that the attending physician is entitled to fair compensation for professional services he renders, but he should not exploit his patient by accepting a markup or profit on services rendered by a laboratory. When an attending physician includes in his bill to the patient services performed by a clinical laboratory, the bill should fully disclose the exact amount of the laboratory charge.

The House adopted the management survey report of Cresap, McCormick and Paget and established a system of assigning priority to activities and programs within the AMA.

Great concern was expressed about the large numbers of physicians who are non-members of the AMA. The House directed the Board of Trustees to study this problem and make effective recommendations for its correction.

Arizona's two resolutions fared well. The first called for the AMA to actively participate in a national anti-smoking campaign. This resolution was combined with two other similar resolutions and adopted by the House.

The second Arizona resolution disapproved the removal of drugs from the market on the basis of NAS/NRS panel reports without opinions of practicing physicians and urged that appropriate corrective legislation be introduced. This resolution was supported by your delegation alone in the reference committee hearing; no opposition or other support was voiced. The committee recommended referral to the Board of Trustees. By House action their report was amended to require the Board to report progress on the resolution at the next clinical session in Denver.

The elections were exciting as usual. Dr. Walter C. Bornemeier, a Chicago surgeon and Speaker of the House for the last three years, was elected President-Elect. Dr. M. Louise Gloeckner, a General Practitioner and the first woman to hold high office in the AMA, was elected Vice-President. Dr. Russell D. Roth, a Urologist, was elected Speaker of the House. All were unopposed.

Dr. Carl Hoffman, a Urologist, was elected to the Board of Trustees seat vacated by Dr. Edward Annis. Dr. J. Frank Walker, a Radiologist, was victorious in a four candidate race for the office of Vice Speaker. Your Arizona delegation was pleased to support both Dr. Hoffman and Dr. Walker in their close elections.

On Thursday, the fifth day, the House proclaimed its last "Aye" and departed the Americana. They were five vital, exciting days with demonstrations, speeches, Apollo XI, long hours of reference committee hearings and interminable House sessions. There were smoke filled rooms, whisky, icy beer, hors d'oeuvres and hamburgers, even Fresca for the fat boys. And more than 850 members of the ubiquitous press mingled, observed, interviewed and popped flash bulbs.

The official chronicle of the convention will eventually appear in JAMA. But the smell and taste, the sense and guts of the proceedings may not be explicit on those finely printed pages.

How can we do a better job? We must deliver health care to the millions who are not getting it. Shall we as health providers inevitably become totally subservient to the government because health is a basic right? Too many practicing physicians reject membership in the AMA because they disagree with its policies. The responsible medical students and young doctors are unhappy with what they consider archaic philosophies. (Average age of the House of Delegates: 62.) The public thinks the AMA is opposed to expanding health care. When Dr. Dorman, our new president, was asked on national television his opinion of the AMA image, he replied in a word: "Poor."

These are the core issues that pique the AMA and importune action. They cannot be resolved by default.

Look what happened at this 118th Annual Convention. Your 242 Delegates listened, argued, and then:

—Pledged dynamic leadership to improve health care of the poor.

—Gave top priority to the problem of rising cost of medical care.

—Proclaimed that every citizen has a basic right to adequate medical care.

—Endorsed the necessity of the peer review concept in providing high quality health services at a reasonable cost.

—Endorsed federal support to medical schools.

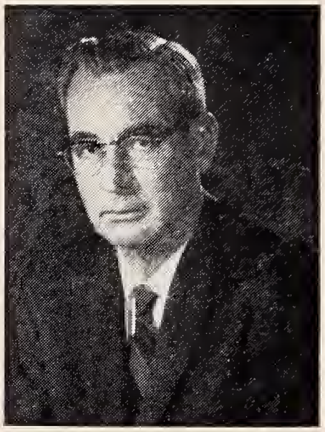
—Outlined programs to help get Medicaid off its back.

—Urged voluntary health insurance and comprehensive health planning at the community level.

Clearly these actions auger change within the AMA — a lean from arch conservatism toward moderation. And clearly we must change if we are to regain preeminence as health providers and properly deliver our superb product to every citizen.

D.T.C.

A copy of the actions taken by the AMA House of Delegates can be obtained by contacting Bruce E. Robinson at ArMA headquarters.



William B. McGrath, M.D.

LANDLORD – PART I

The commonest cause of death is to feel unwelcome in the world.

During second world war and with the bombings of great cities, many children had to be put in orphanages. It was possible to take care of what were thought to be their basic needs: food, warmth, sanitation, medical supervision. In the protracted emergency not much more could be be done for them.

Nor did the authorities realize and spell out the children's crucial need of comforting. Given everything else except physical tenderness, some infants and even older children lost interest in their surroundings, grew listless and simply died. The real cause of death could not be shown at necropsy nor seen under the microscope.

Pediatricians and child psychologists have given this matter some warranted publicity. And its corollary applicability to the care of the aged is readily understood. The very young and the very old cannot seek their own nourishment, and this they have in common. Their helpless dependency can be recognized. And when a person's helplessness is visible, then others are released from shyness and free to volunteer.

The need to be welcomed is not at all diminished in adolescence. The trouble is that false pride keeps it from being openly expressed. Our modern affluence and our "enlightened" minimum wage and child labor laws conspire to deny the young people any opportunity to be of service, to earn their welcome. No wonder they are attacking our culture or turning their backs on it.

A few of the tragedies of adolescence will be be mentioned to illustrate our theme. The incidence of suicide is rising. Only the schizophrenic is self-sufficient, or tries to be; and unattended he, too, will die. Or consider the sorrow of the homosexual: "Maybe if I had been born a girl, you might have accepted me." Will he not put himself in dangerous situations, prowling the streets or picking up hitch-hikers, unconsicously soliciting his own destruction? Homosexuals are the most numerous victims of murder. Anorexia nervosa and some cases of ulcerative colitis and all the psychosomatic diseases come to mind.

The need to feel welcome is just as strong and elemental in the ordinary adult. Fatal accidents result from literal care-lessness; and no-one knows which ones were more or less deliberately contrived by individuals who were about to lose face. Patients who do not value themselves or who feel poorly valued will neglect their health, and they will not desist from drinking or smoking or otherwise dulling their vitality and hastening their deaths. Anyone who is not at ease is vulnerable to dis-ease. Many persons are obviously working themselves to death, and not unconsciously, because they can never earn a sustained feeling of welcome.

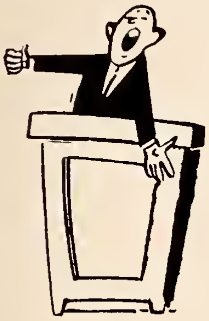
Physicians, on the other hand, are constant witnesses to the healing force of hospitality. A pill dispensed with kindness takes on a hundred-fold increase in efficacy. Untold numbers of people come in mute desperation to the clinic or to the doctor's office as a last resort, a sanctuary, when everywhere else they have been wounded or ignored.

To be unsure of one's welcome does cause a most unpleasant nervousness or aprehension. And the most crushing physical sickness of all is that of rejection. In our prejudices, in our subtle ostracisms and in our pitiless indifference, perhaps all of us are partly guilty of negligent homicide.

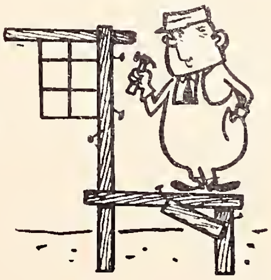
The lesson speaks for itself — but not just to doctors! All those who decry the prevalence of illness and the cost of medical care could begin to do something immeasurably helpful. They could consciously apply some of our knowledge and share some of our responsibility. We are referring to every official, every shopkeeper, every executive. We are appealing to all the "landlords" of society. Wherever there are vestibules or waiting rooms of any kind, there are people who will die too soon if they are not somehow made to feel welcome in the world. Awareness of this is not just charity; it can be an extremely important contribution to preventive medicine and public health.

Topics Of Current Medical Interest

AUGUST 27, 1969 — UP SHE GOES — AUGUST 13, 1969



SCIENTIFIC PAPERS



SCIENTIFIC EXHIBITS

FOR THE 1970 ANNUAL MEETING
APRIL 21 - 25, 1970

EXHIBITS:

The Scientific Assembly Committee has arranged to expand and improve the facilities for scientific exhibits at the 1970 annual meeting. You are most cordially invited to develop an exhibit for the 1970 meeting. Send a brief description to:

Chairman — Scientific Assembly Committee
Arizona Medical Association
4601 N. Scottsdale Road
Scottsdale, Arizona 85251

Booth Spaces are 8′ wide and 6′ deep (two booths may be used if your exhibit is larger). All applications for exhibit space MUST BE MAILED BY DECEMBER 1, 1969. Set-up details will be mailed to you about one month before the meeting.

All Medical Directors are urged to encourage Interns, Residents and Fellows to participate.

(please indicate in your letter of application if more than one booth space will be required for your exhibit)

●●●●●●

PAPERS:

Again this year the Arizona Medical Association is soliciting papers from Arizona physicians for presentation at our Annual Meeting in April, 1970. We are particularily interested in having the Directors of Medical Education in our state's hospitals encourage the participation of their Interns, Residents and Fellows. The papers should be approximately one-half hour in length. A brief abstract should be mailed to:

Chairman — Scientific Assembly Committee
Arizona Medical Association
4601 N. Scottsdale Road
Scottsdale, Arizona 85251

The deadline for consideration is December 1, 1969.

●●●●●●

Should you have questions either about exhibits or papers please feel free to contact Bruce E. Robinson at ArMA headquarters. . .

CLINICAL CARDIOLOGY

DECEMBER 8-13, 1969

Del Webb's TowneHouse, Phoenix, Arizona

Presented by: The American College of Cardiology and The Institute for Cardiovascular Diseases, Good Samaritan Hospital, Phoenix, Arizona

An intensive six-day program covering in depth selected fields in cardiovascular diseases. The program is oriented toward practical application of diagnostic techniques, basic understanding of pathophysiology of heart disease and medical and surgical management of the most common problems in cardiology. The participants will be encouraged to become involved with interpretation of records on informal workshop type of sessions planned for the evenings. This course is intended for those who want an extensive and detailed discussion of the current aspects of cardiovascular diagnoses and therapy.

FACULTY

Program Director:

ALBERTO BENCHIMOL, M.D., F.A.C.C., Director, Institute for Cardiovascular Diseases, Good Samaritan Hospital, Phoenix, Ariz.

Guest Faculty:

WILLIAM DORSON, Ph.D., Associate Professor in Chemical Engineering, Arizona State University, Tempe, Ariz.

DARRELL D. FANESTIL, M.D., Assistant Professor of Medicine, The University of Kansas School of Medicine, Kansas City, Kans.

ALBERT A. KATTUS, JR., M.D., Professor of Medicine and Chief, Division of Cardiology, University of California, Los Angeles School of Medicine, Los Angeles, Calif.

JEROME H. KAY, M.D., F.A.C.C., Associate Professor of Surgery, The University of Southern California School of Medicine and Chief of Thoracic Surgery, St. Vincent's Hospital, Los Angeles, Calif.

DEAN T. MASON, M.D., F.A.C.C., Professor of Medicine and Physiology and Chief, Section of Cardiopulmonary Medicine, University of California, Davis School of Medicine, Davis, Calif.

PHILIP SAMET, M.D., F.A.C.C., Chief, Division of Cardiology, Mount Sinai Hospital, Miami Beach, Fla.

ARNOLD M. WEISSLER, M.D., F.A.C.C., Professor of Medicine and Director, Division of Cardiology, The Ohio State University College of Medicine, Columbus, Ohio

Institute for Cardiovascular Diseases, Good Samaritan Hospital Faculty:

MARIAN E. MOLTHAN, M.D., F.A.C.C., Associate Director

JOSEPH EHRLICH, M.D., F.A.C.C., Consultant in Cardiology

ALLEN ASENDORF, M.D., Postgraduate Fellow

R. VASQUEZ IBARRA, M.D., Postgraduate Fellow

SHUZO MATSUO, M.D., Research Fellow

STEPHEN TIO, M.D., Postgraduate Fellow

ADVANCE REGISTRATION IS REQUIRED. FOR ADDITIONAL INFORMATION AND APPLICATION CONTACT:

William D. Nelligan, Executive Director, American College of Cardiology, 9650 Rockville Pike, Bethesda, Md. 20014

THE ACADEMY OF PSYCHOSOMATIC MEDICINE
SIXTEENTH ANNUAL MEETING

November 19-23, 1969

Mountain Shadows, Scottsdale, Arizona

THEME: PSYCHIATRY IN THE DAILY PRACTICE OF MEDICINE

For further information and pre-registration material contact:

Edwin Dunlop, M.D.
Executive Secretary
150 Emory Street
Attleboro, Mass. 02703

6TH NATIONAL CANCER CONFERENCE – NOTES

September 1968, Denver

MAMMOGRAPHY IN THE MANAGEMENTS OF BREAST CANCER

95% of the patients with breast cancer make their own discovery of the tumor of the breast, only 10% of them survive 10 years. He believes that every biopsy should be preceded by a mammogram. In their series 10% of the breast cancer was discovered by mammography. This procedure, mammography, should not interfere with the clinical necessity of doing a biopsy. In their patients who have had mammography, they have discovered twice as many carcinomas in the second breast as have been reported previously in routine follow-up studies. He reports in contrast to Dr. Urban a 15% involvement in the opposite breast and in 75% of the cases this is a secondary primary carcinoma, 3% of their patients have simultaneously breast cancer in both breasts.

Robert L. Egan, M.D., Chief
Mammography Section, Emory
University School of Medicine,
Atlanta, Georgia

Coming out of a depression.

And it can often begin to happen in 3 to 5 days with an antidepressant like Pertofrane. There's a lifting of depressed mood . . . a restoration of psychomotor activity. Patients usually begin to cope, work, maybe play, even enjoy.

It's not all beautiful. Sometimes there are side effects. And not everybody can take the drug. It may even be a slow process. But along with the care and comfort you give depressed patients, consider Pertofrane. Then consider the respons

Please read the prescribing information for full details on contraindications, warnings, precautions, adverse reactions and dosage. It's summarized on the left.

Pertofrane®

desipramine hydrochloride

New 50-mg. capsules now available.

Pertofrane® desipramine hydrochloride

Indication: Mental depression.

Contraindications: Do not use MAO inhibitors concomitantly or within 2 weeks of the use of this drug. Hyperpyretic crises or severe convulsive seizures may occur with such combinations; potentiation of adverse reactions can be serious or even fatal.

When substituting Pertofrane in patients receiving an MAO inhibitor, allow an interval of at least 14 days. Initial dosage in such patients should be low and increases should be gradual and cautiously prescribed.

The drug is contraindicated following recent myocardial infarction and in patients with a known hypersensitivity to tricyclic antidepressants.

Warning: Activation of psychosis may occasionally be observed in schizophrenic patients. Due to atropine-like effects and sympathomimetic potentiation, use only with the greatest care in patients with narrow-angle glaucoma or urethral or ureteral spasm.

Do not use in patients with the following conditions unless the need outweighs the risk: severe coronary heart disease with EKG abnormalities, progressive heart failure, angina pectoris, paroxysmal tachycardia and active seizure disorder (may lower seizure threshold).

Desipramine and the parent compound, imipramine, have been shown to block the action of guanethidine and related adrenergic neuron-blocking agents.

Hypertensive episodes have been observed during surgery.

The concurrent use of other central nervous system drugs or alcohol may potentiate adverse effects. Since many such drugs may be used during surgery, desipramine should be discontinued prior to elective procedures.

Caution patients on the possibility of impaired ability to operate a motor vehicle or dangerous machinery.

Do not use in women who are or may become pregnant unless the clinical situation warrants the potential risk, and do not use in patients under 12 years of age.

Because of increased sensitivity to the drug, use lower than normal dosage in adolescent and geriatric patients.

Precautions: Potentially suicidal patients require careful supervision and protective measures during therapy. Discontinuation of the drug may be necessary in the presence of increased agitation and anxiety shifting to hypomanic or manic excitement.

Atropine-like effects may be more pronounced (e.g. paralytic ileus) in susceptible patients and in those receiving anticholinergic drugs (including antiparkinsonism agents).

Prescribe cautiously in hyperthyroid patients and in those receiving thyroid medications; transient cardiac arrhythmias have occurred in rare instances.

Periodic blood and liver studies should supplement careful clinical observations in all patients undergoing extended courses of therapy.

Adverse Reactions: The following have been reported: *Nervous System:* dizziness, drowsiness, insomnia, headache, disturbed visual accommodation, tremor, unsteadiness, tinnitus, paresthesias, changes in EEG patterns, epileptiform seizures, mild extrapyramidal activity, falling and neuromuscular incoordination. A confusional state (with such symptoms as hallucinations and disorientation), particularly in older patients and at higher dosage, may require discontinuation of the drug. *Gastrointestinal Tract:* anorexia, dryness of the mouth, nausea, epigastric distress, constipation and diarrhea. *Skin:* skin rashes (including photosensitization), perspiration and flushing sensations. *Liver:* rare cases of transient jaundice (apparently of an obstructive nature) and liver damage. If jaundice or abnormalities in liver function tests occur, discontinue the drug and investigate. *Blood Elements:* bone-marrow depression, agranulocytosis, thrombocytopenia and purpura. If these occur, discontinue the drug. Transient eosinophilia has been observed. *Cardiovascular System:* orthostatic hypotension and tachycardia. Carefully supervise patients requiring concomitant vasodilating therapy, particularly during initial phases. *Genitourinary System:* urinary frequency or retention and impotence. *Endocrine System:* occasional hormonal effects, including gynecomastia, galactorrhea and breast enlargement, and decreased libido and estrogenic effect. *Sensitivity:* urticaria and rare instances of drug fever and cross-sensitivity with imipramine.

Dosage: All patients except geriatric and adolescent: 50 mg. t.i.d. (150 mg. daily). Dosage may be increased up to 200 mg. daily. Geriatric and adolescent patients should usually be started with lower dosage (25 to 50 mg. daily) and may not tolerate higher doses. Dosage may be increased up to 100 mg. daily.

Lower maintenance dosages should be continued for at least 2 months after obtaining a satisfactory response.

Mild anxiety and agitation which may accompany depression usually remit as the depression responds. Occasionally, however, a sedative or tranquilizer may be indicated.

Availability: Maroon and pink capsules of 50 mg. in bottles of 100; pink capsules of 25 mg. in bottles of 100 and 1000.
(B)46-530-G

For complete details, please see the full prescribing information.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
Ardsley, New York 10502

It's beautiful!

heavenly relief
for unearthly cough

Benylin®
EXPECTORANT

Each fluidounce contains: 80 mg. Benadryl® (diphenhydramine hydrochloride, Parke-Davis); 12 grains ammonium chloride; 5 grains sodium citrate; 2 grains chloroform; 1/10 grain menthol; and 5% alcohol. An antitussive and expectorant for control of coughs due to colds or of allergic origin, BENYLIN EXPECTORANT is the leading cough preparation of its kind. BENYLIN EXPECTORANT tends to inhibit cough reflex... soothes irritated throat membranes. And its not-too-sweet, pleasant raspberry flavor makes BENYLIN EXPECTORANT easy to take. PRECAUTIONS: Persons who have become drowsy on this or other antihistamine-containing drugs, or whose tolerance is not known, should not drive vehicles or engage in other activities requiring keen response while using this preparation. Hypnotics, sedatives, or tranquilizers if used with BENYLIN EXPECTORANT should be prescribed with caution because of possible additive effect. Diphenhydramine has an atropine-like action which should be considered when prescribing BENYLIN EXPECTORANT. ADVERSE REACTIONS: Side reactions may affect the nervous, gastrointestinal, and cardiovascular systems. Drowsiness, dizziness, dryness of the mouth, nausea, nervousness, palpitation, and blurring of vision have been reported. Allergic reactions may occur. PACKAGING: Bottles of 4 oz., 16 oz., and 1 gal.

Parke, Davis & Company
Detroit, Michigan 48232

PARKE-DAVIS

410R69

now he can cope...

thanks to

Butisol SODIUM®
(SODIUM BUTABARBITAL)

the "daytime sedative" for everyday situational stress

When stress is situational—environmental pressure, worry over illness—the treatment often calls for an anxiety-allaying agent which has a prompt and predictable calming action and is remarkably well tolerated. BUTISOL SODIUM (sodium butabarbital) meets this therapeutic need.

After 30 years of clinical use . . . still a first choice among many physicians for dependability, safety and economy in mild to moderate anxiety.

Contraindications: Porphyria or sensitivity to barbiturates.

Precautions: Exercise caution in moderate to severe hepatic disease. Elderly or debilitated patients may react with marked excitement or depression.

Adverse Reactions: Drowsiness at daytime sedative dose levels, skin rashes, "hangover" and systemic disturbances are seldom seen.

Warning: May be habit forming.

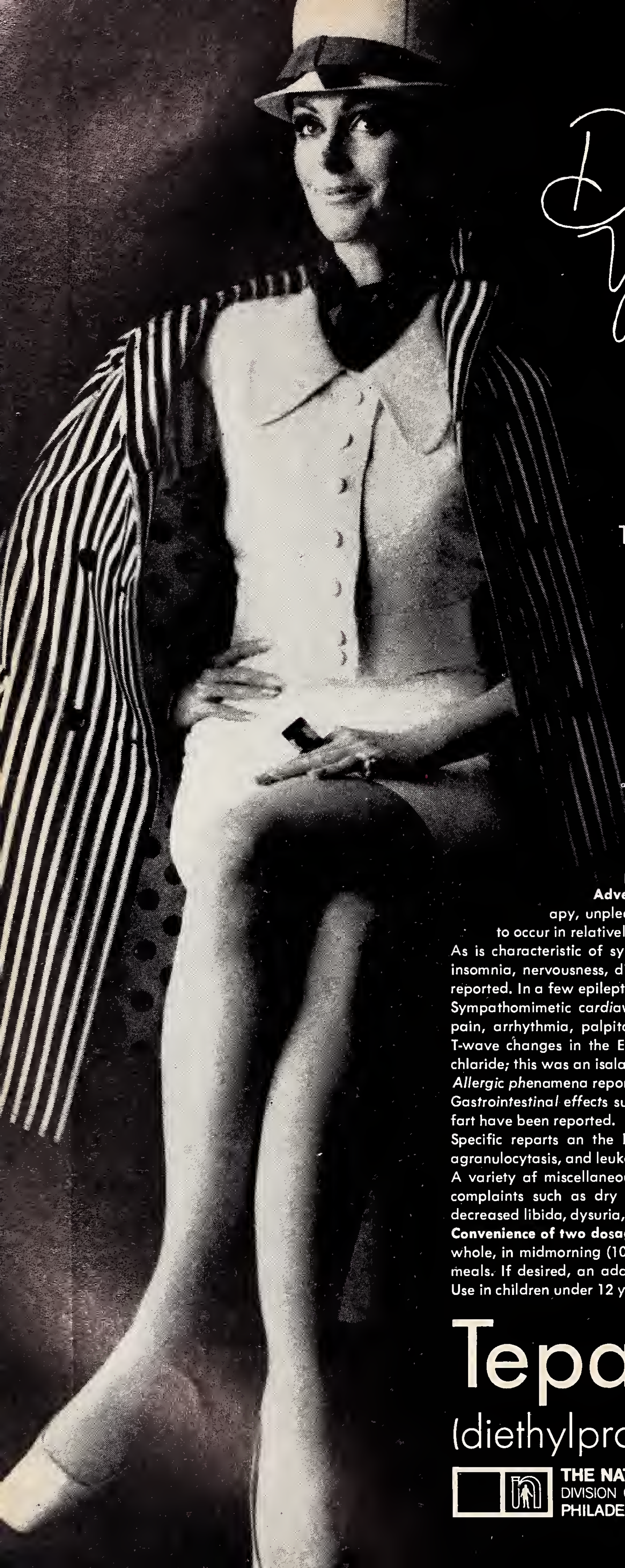
Usual Adult Dosage: As a daytime sedative, 15 mg. (¼ gr.) to 30 mg. (½ gr.) t.i.d. or q.i.d.

Available for daytime sedation: Tablets, 15 mg. (¼ gr.), 30 mg. (½ gr.); Elixir, 30 mg. per 5 cc. (alcohol 7%).

BUTICAPS® [Capsules BUTISOL SODIUM (sodium butabarbital)] 15 mg. (¼ gr.), 30 mg. (½ gr.).

McNEIL

McNeil Laboratories, Inc., Fort Washington, Pa.



Dear Doctor,
You made me
what I am today-
a whole lot
slimmer!

TEPANIL—the right start in support of the weight-control program *you* recommend. It reduces the appetite. Doesn't kill it. Weight loss is significant—gradual—yet there is a relatively low incidence of CNS stimulation. Because TEPANIL works on the appetite, not on the "nerves."

Contraindications: Concurrently with MAO inhibitors, in patients hypersensitive to this drug; in emotionally unstable patients susceptible to drug abuse.

Warning: Although generally safer than the amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence.

As is characteristic of sympathomimetic agents, it may occasionally cause *CNS effects* such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptics an increase in convulsive episodes has been reported.

Sympathomimetic *cardiovascular effects* reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others.

Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema.

Gastrointestinal effects such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported.

Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia.

A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

Convenience of two dosage forms: TEPANIL Ten-tab tablets: One 75 mg. tablet daily, swallowed whole, in midmorning (10 a.m.); TEPANIL: One 25 mg. tablet three times daily, one hour before meals. If desired, an additional tablet may be given in midevening to overcome night hunger. Use in children under 12 years of age is not recommended.

Tepanil® Ten-tab®

(continuous release form)

(diethylpropion hydrochloride)

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON-MERRELL INC.
PHILADELPHIA, PENNSYLVANIA 19144

T-918A U.S. PATENT NO. 3,001,910 5/69

Ornade® Spansule® brand of sustained release capsules

Trademark
Each capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate); 50 mg. of phenylpropanolamine hydrochloride; 2.5 mg. of isopropamide, as the iodide.

Prompt relief from nasal congestion and hypersecretion due to colds.

Before prescribing, see complete prescribing information in SK&F literature or *PDR*.
Contraindications: Glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloroduodenal or bladder neck obstruction.
Precautions: Use cautiously in the presence of hypertension, hyperthyroidism, coronary artery disease; warn vehicle or machine operators of possible drowsiness.
Usage in Pregnancy: Use in pregnancy, nursing mothers and women who might bear children only when potential benefits have been weighed against possible hazards.
Note: The iodine in isopropamide iodide may alter PBI test results and will suppress I^{131} uptake; discontinue 'Ornade' one week before these tests.
Adverse Reactions: Drowsiness; excessive dryness of nose, throat or mouth; nervousness; insomnia. Other known possible adverse reactions of the individual ingredients: nausea, vomiting, diarrhea, rash, dizziness, fatigue, tightness of chest, abdominal pain, irritability, tachycardia, headache, incoordination, tremor, difficulty in urination. Thrombocytopenia, leukopenia and convulsions have been reported.
Supplied: Bottles of 50 capsules.

One capsule q12h for round-the-clock relief

SK&F **Smith Kline & French Laboratories**

helps restore normal motility and tone

CANTIL®

(mepenzolate bromide)

Diarrhea and other symptoms of common G.I. disorders can often be curbed with Cantil (mepenzolate bromide), bringing welcome relief to the harassed patient. Relatively specific for the hyperactive colon, it helps reduce diarrhea, pain and spasm with minimal effect on other viscera. Cantil (mepenzolate bromide) is indicated whenever these symptoms are associated with irritable colon, gastroenteritis, diverticulitis, and mild to moderate ulcerative colitis.

It is an anticholinergic drug without narcotic properties. Side effects are usually mild.

LAKESIDE

CONTRAINDICATIONS: Sensitivity to Cantil® (mepenzolate bromide), glaucoma, G.I. or G.U. obstruction, toxic megacolon. **WARNINGS:** Possibility of adverse reactions in advanced severe ulcerative colitis and atypical agitated reactions to phenobarbital in the elderly (Cantil with Phenobarbital). **PRECAUTIONS:** Cantil is of adjunctive use only; treatment of the underlying condition is indicated, be it organic or functional. Observe caution in conditions known to be incompatible with atropine-like drugs, e.g., open-angle glaucoma or prostatic hypertrophy. **ADVERSE EFFECTS:** Dry mouth; blurred vision; constipation; nausea; vomiting; bloating; dizziness; urinary retention. All are anticholinergic effects and usually tolerable. Habituation and idiosyncratic reactions to phenobarbital (Cantil with Phenobarbital) are possible, as is generalized rash. **DOSAGE:** One or two tablets three times a day and one or two at bedtime usually provide prompt relief. Cantil with Phenobarbital may be prescribed if sedation is required. **HOW SUPPLIED:** CANTIL (mepenzolate bromide)—25 mg. per scored tablet. Bottles of 100 and 250. CANTIL with PHENOBARBITAL—containing in each scored tablet 16 mg. phenobarbital (warning: may be habit forming) and 25 mg. mepenzolate bromide. Bottles of 100 and 250.

LAKESIDE LABORATORIES, INC., Milwaukee, Wisconsin 53201

Because any
urologic infection
can be serious,
BREON introduces
potent therapy

for the strong start and a fast finish...

"...a significant gap appears to have been closed in the armory of drugs available to the urologist."[1]

Bacteriuria and symptoms can be eliminated within 48 to 72 hours; susceptible infection often in 10 to 14 days.

before your "minor" becomes a major problem

choice initial treatment for urinary infections

Cybis® (nalidixic acid) provides prompt broad gram-negative bactericidal activity at normal urinary pH range that can eradicate troublesome *E. coli,* Aerobacter and Proteus. A good starting drug, it can effectively accelerate management of infection due to sensitive organisms.

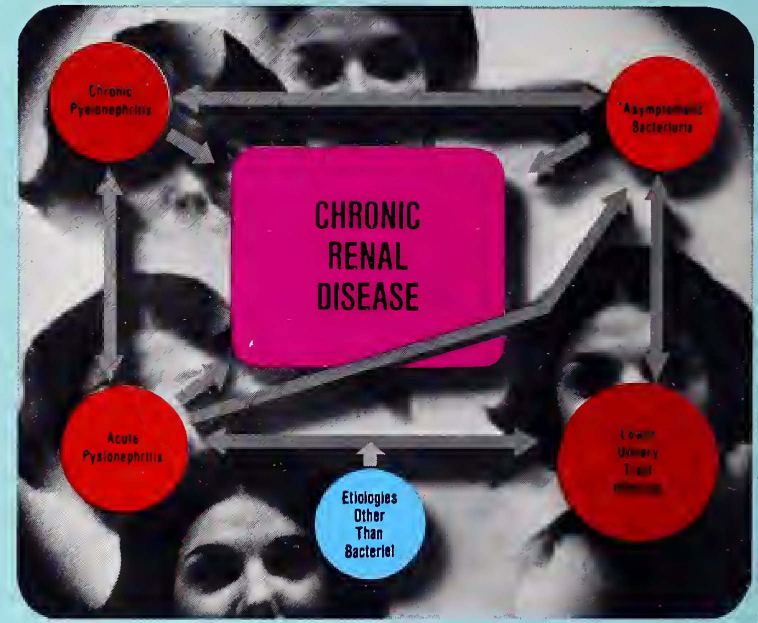
essential control within the primary 72-hour cycle

In cases of acute infection due to susceptible organisms, Cybis works well toward the rapid clearing of disease when obstruction is absent or can be relieved. Within 48 to 72 hours, symptoms are frequently eased and bacteriuria eliminated. Susceptible infection is often eradicated in 10 to 14 days.

blocks the young female progression of infection

Cybis can be useful in naturally susceptible young female patients with new or well-established urinary disturbances. Combining rapid potency with relative freedom of serious side reactions and toxicity, the drug can be of particular value in preventing higher tract involvement or blocking the possible continuum of disease. (See Chart)

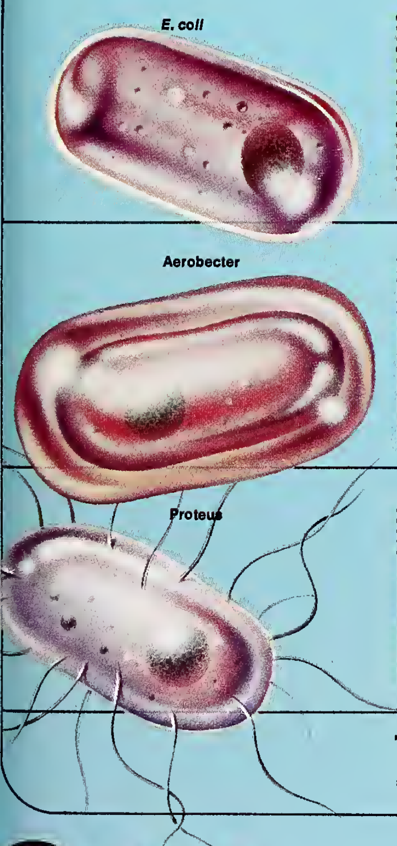
Kinetic Relationship of Acute and Chronic Bacterial Pyelonephritis to Chronic Renal Disease[2]



consistent activity against 706 gram-negative strains

In vitro testing of *E. coli*, Aerobacter and Proteus species showed better than 90% sensitivity to nalidixic acid[3] (See Table)

Better Than 90% Sensitivity Among 3 Common Urinary Invaders



	Strains	Sensitivity to Nalidixic Acid	Sensitivity
E. coli	413	394	95%
Aerobecter	148	133	90%
Proteus	145	129	89%
TOTAL 706 57 of 88 Pseudomonas species were resistant		Average	91%

References: 1. Reimann-Hunziker, R. and Reimann-Hunziker, G. J.: *Praxis* 53:15, Jan. 9, 1964. 2. Sanford, J. P.: *Med. Times* 96:715, July 1968. 3. Reese, L.: *Canad. M. A. J.* 92:394-397, Feb. 20, 1965.

Cybis®
(nalidixic acid)

for the strong start and a fast finish... in cystitis, pyelonephritis, prostatitis, urethritis

Before prescribing, please consult complete product information, a summary of which follows on the next page, including indications, warning, precautions, adverse reactions and dosage.

Summary of prescribing information

Indications: Urinary tract infections in which species of sensitive gram-negative bacteria are predominant, particularly *Proteus, Escherichia coli, Aerobacter, Klebsiella,* and certain strains of *Pseudomonas.* Gram-positive bacteria are less sensitive to Cybis but favorable clinical results have been observed.

Warning: Use in Pregnancy. This drug is not recommended in the first trimester of pregnancy. However, it has been used in several patients during the last two trimesters without producing apparent ill effects in either mother or fetus.

Precautions: Although prolonged treatment with Cybis has been generally well tolerated, as with all new drugs it is advisable to carry out blood, renal, and liver function tests periodically if treatment is continued for more than one or two weeks. The dosage recommended for adults and children should not be arbitrarily doubled unless under the careful supervision of a physician. **It should be used with caution in patients with liver disease, epilepsy, or severe cerebral arteriosclerosis, and in patients in whom kidney function is severely impaired.** Patients should be cautioned to avoid unnecessary exposure to direct sunlight while receiving Cybis and, if a photosensitivity reaction occurs, therapy should be discontinued.

During treatment microorganisms may develop resistance to this drug. Resistant bacteria, not previously present or identified, may emerge. Cultures should be taken and bacterial sensitivity tests made periodically, particularly if the clinical response is unsatisfactory or if a relapse occurs. Should resistance develop, other specific chemotherapy should be instituted; no cross resistance has been observed. If new strains of bacteria that are not sensitive emerge, other effective antibacterial agents may be added. When Benedict's or Fehling's solutions or Clinitest® Reagent Tablets are used to test the urine of patients taking Cybis, a false-positive reaction for glucose may be obtained due to the liberation of glucuronic acid from the metabolites excreted. However, a colorimetric test for glucose based on an enzyme reaction (using, for example, Clinistix® Reagent Strips or Tes-Tape®) does not give a false-positive reaction to Cybis glucuronide.

Adverse reactions: Mainly mild nausea, vomiting, and other gastrointestinal disturbances: less frequently, sleepiness, drowsiness, weakness, headache, dizziness and vertigo, and rarely cholestasis, paresthesia, thrombocytopenia, leukopenia, or hemolytic anemia which in some patients may have been associated with deficiency in activity of glucose-6-phosphate dehydrogenase. Itching, pruritus, rash, urticaria, mild eosinophilia, reversible photosensitivity reactions primarily involving exposed surfaces, and reversible subjective visual disturbances (overbrightness of lights, change in visual color perception, difficulty in focusing, decrease in visual acuity and double vision), occurred occasionally. Reversible increased intracranial pressure with bulging anterior fontanel, papilledema, and headache have been observed occasionally in infants and children. Toxic psychosis and brief convulsions (the latter generally in patients with possible predisposin factors, and both usually associated with excessive dosage) have been recorded in rare instances.

Dosage and administration: *Adults*—Four Gm. d by mouth (2 tablets of 500 mg. four times daily) for c to two weeks. Thereafter, if prolonged treatment is indicated, the dosage may be reduced to two Gm. d (1 tablet of 500 mg. four times daily). *Children*— According to age and weight: approximately *25 mg per pound* of body weight per day, administered in divided doses.

Note: The dosage recommended above for adults a children should not arbitrarily be doubled unless u the careful supervision of a physician. Until further experience is gained, infants under 1 month should be treated with the drug.

How supplied: Tablets of 500 mg., bottles of 50.

Before prescribing, please refer to complete prescribing information.

Cybis®
(nalidixic acid)

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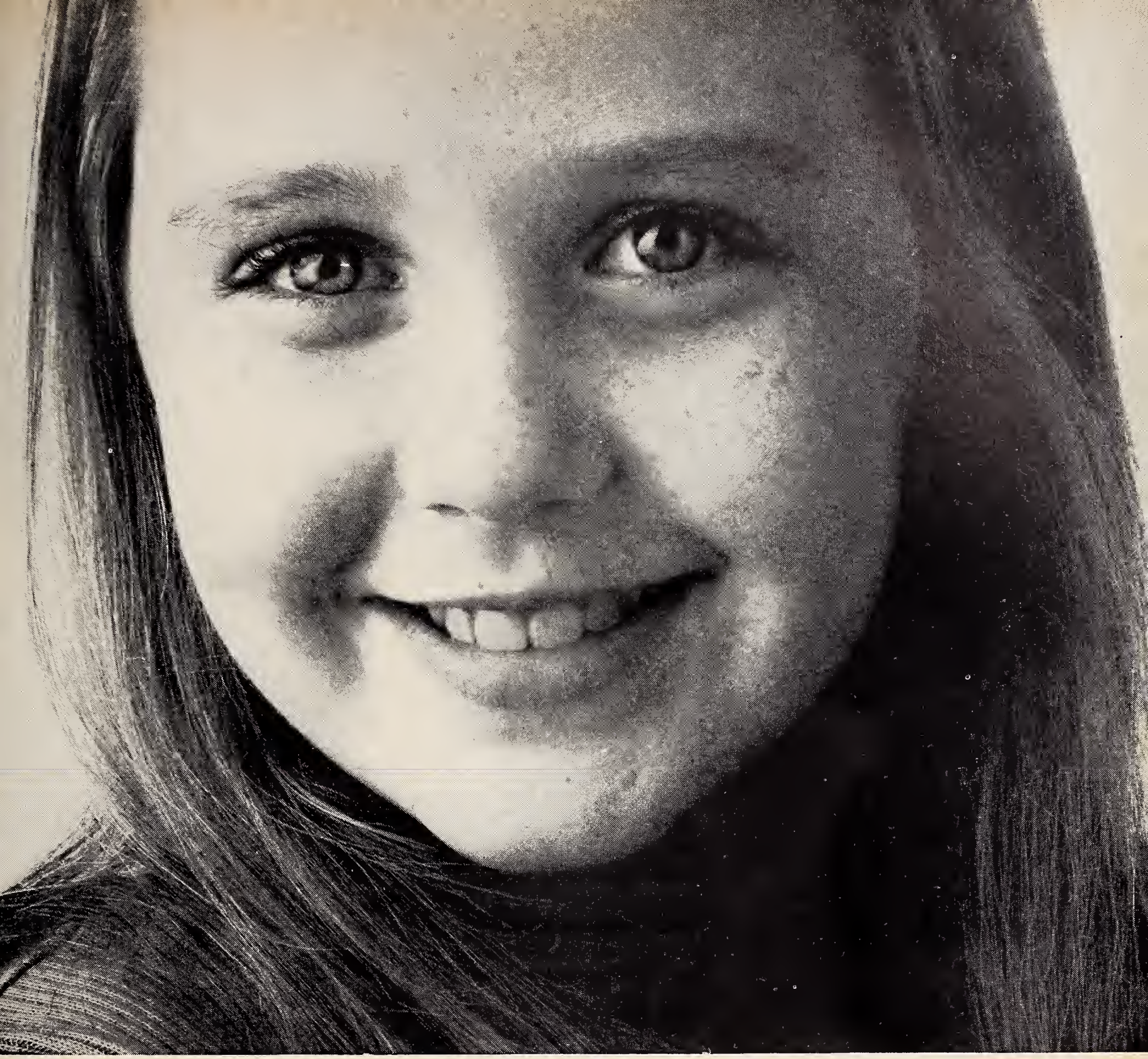

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Warnings: Acute anaphylaxis (may prove fatal unless promptly controlled) is rare but more frequent in patients with previous penicillin sensitivity, bronchial asthma or other allergies. Resuscitative (epinephrine, aminophylline, pressor amines) and supportive (antihistamines, methylprednisolone sodium succinate) drugs should be readily available. Other rare hypersensitivity reactions include nephropathy, hemolytic anemia, leucopenia and thrombocytopenia. In suspected hypersensitivity, evaluation of renal and hematopoietic systems is recommended.
Precautions: In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.
Adverse Reactions: (Penicillin has significant index of sensitization): Skin rashes, ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; serum sickness-like reactions, including chills, fever, edema, arthralgia and prostration. Severe and often fatal anaphylaxis has been reported (see "Warnings").
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Wyeth Laboratories Philadelphia, Pa.

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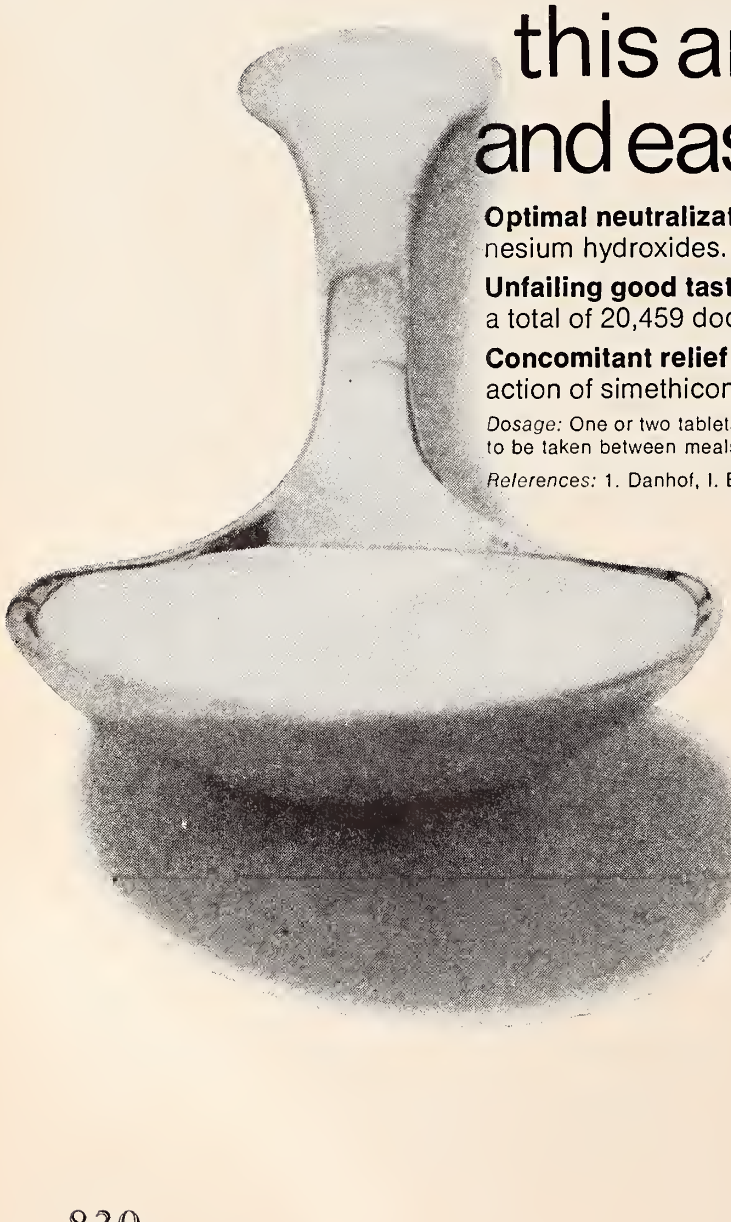

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References: 1. Danhof, I. E.: Report on file. 2. Hoon, J. R.: Arch. Surg. *93*:467 (Sept.) 1966.

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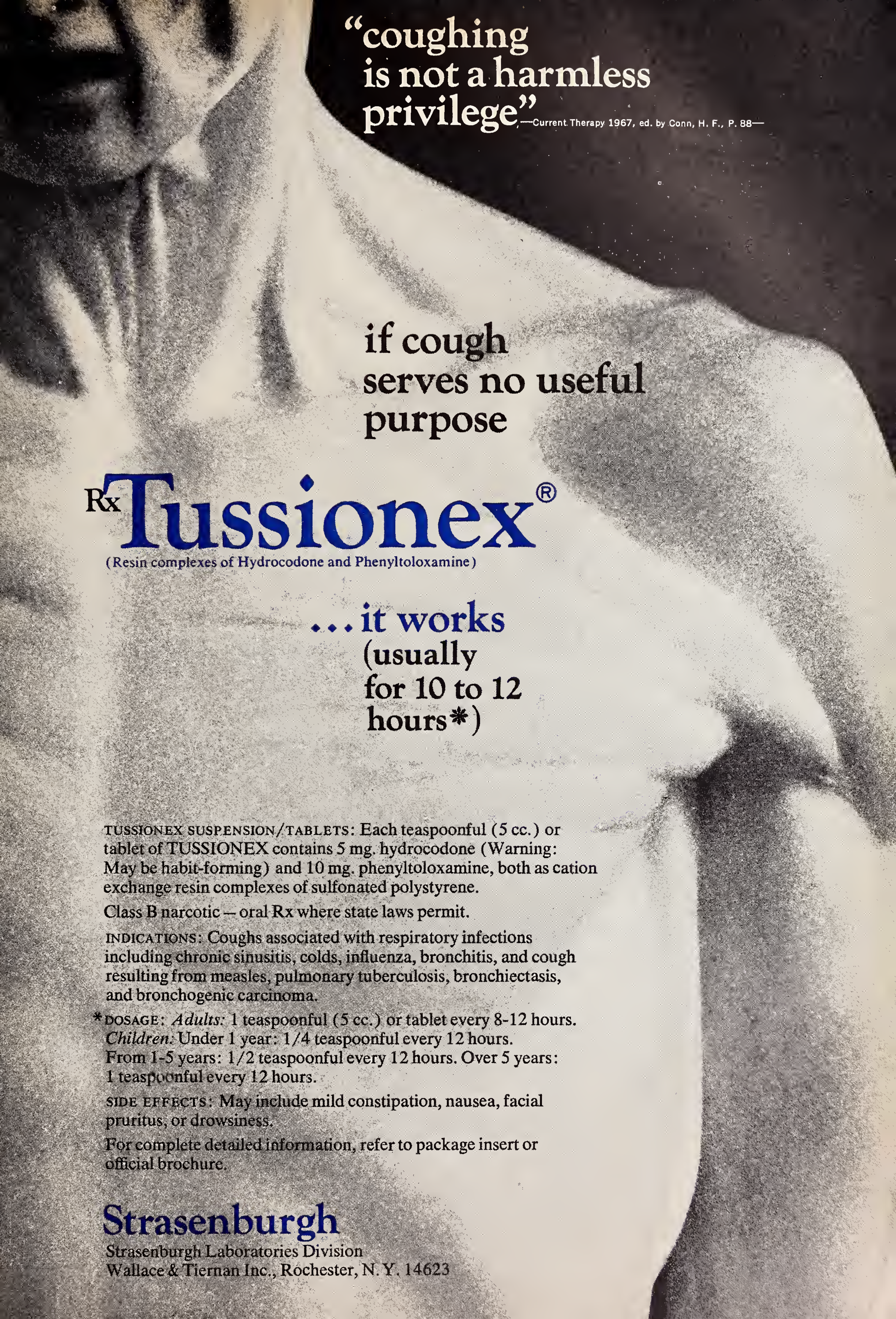
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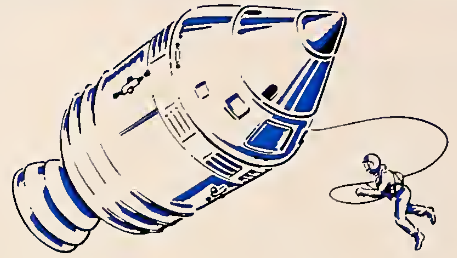

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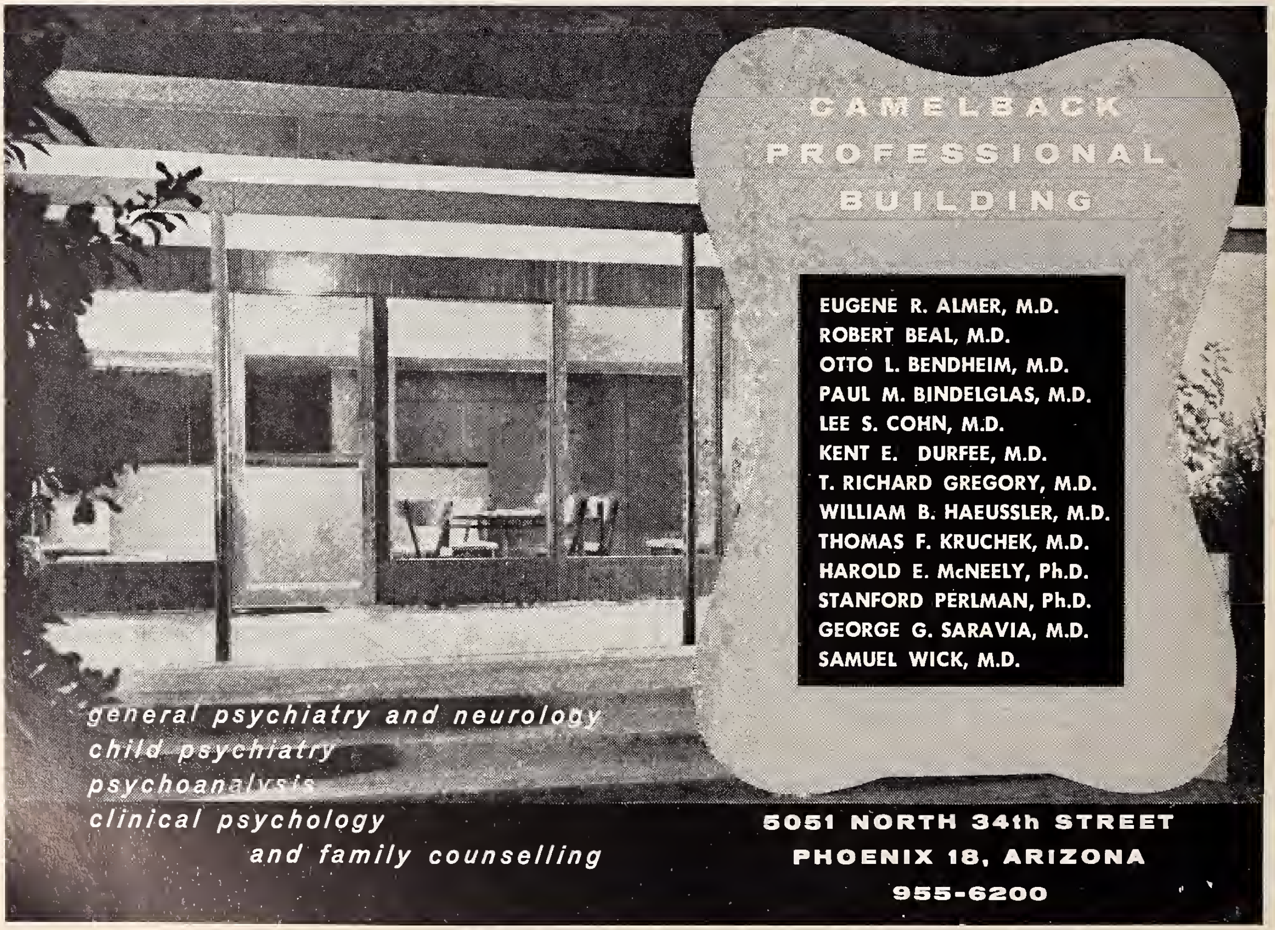

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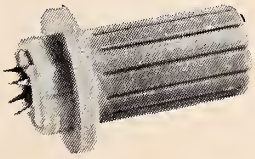

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1. Banov, L.: South. M. J. 57: 328-331 (March) 1964.

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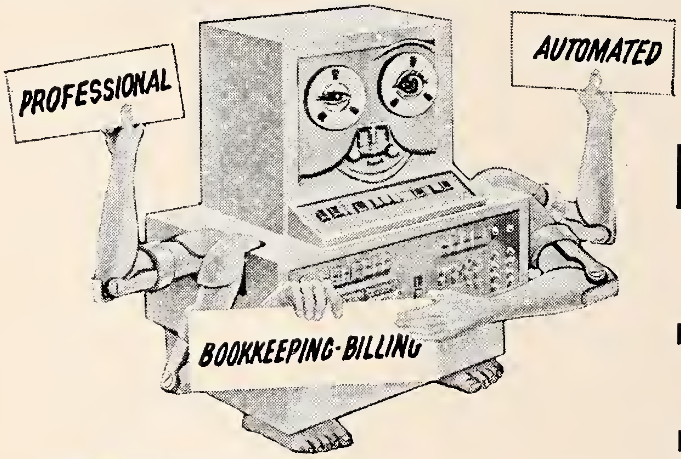

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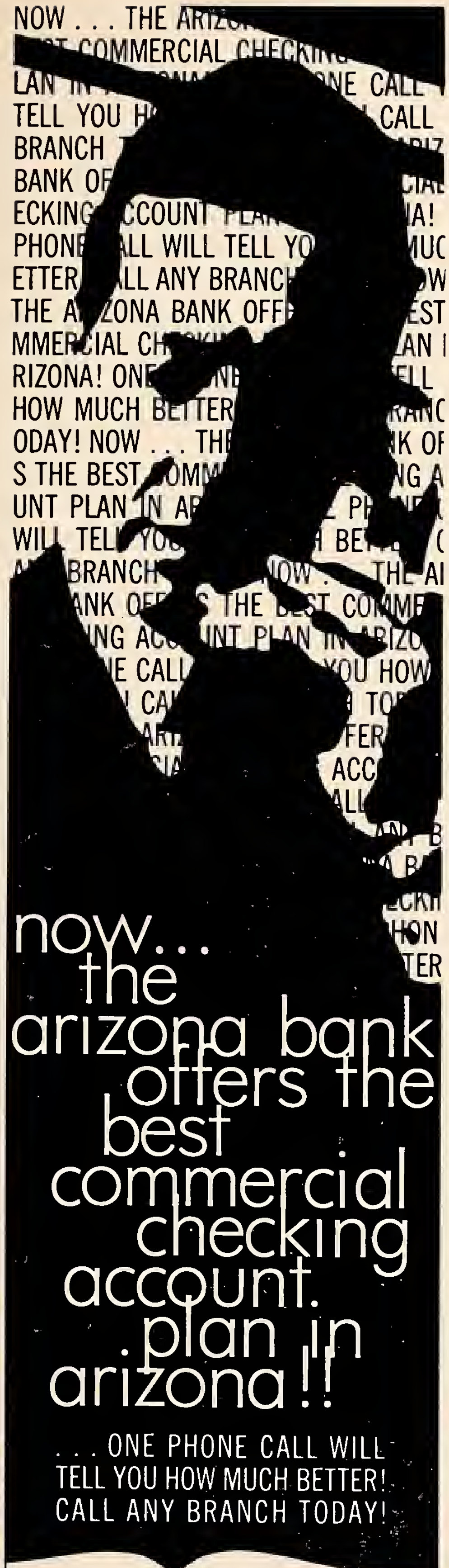

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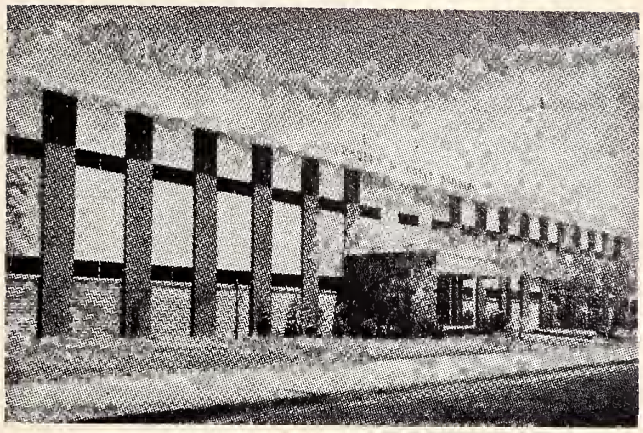

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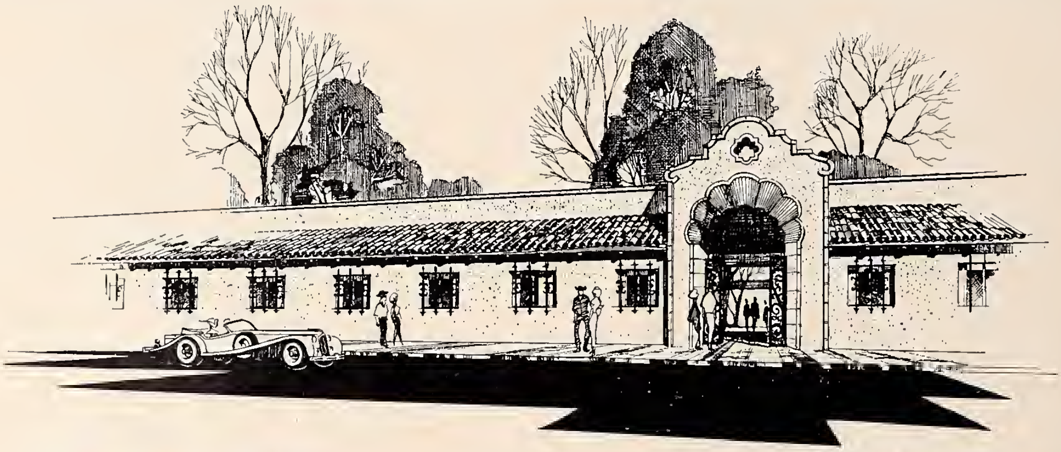

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3 FREQUENCY OF ISSUE: MONTHLY
4 LOCATION OF KNOWN OFFICE OF PUBLICATION *(Street, city, county, state, ZIP code)*: LEBEAU PRINTING CO. 2216 WEST GRANADA ROAD, PHOENIX, ARIZONA 85009
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EDITOR *(Name and address)*: Robert F. Lorenzen, M.D., 4601 N. Scottsdale Road, Scottsdale, Arizona 85251
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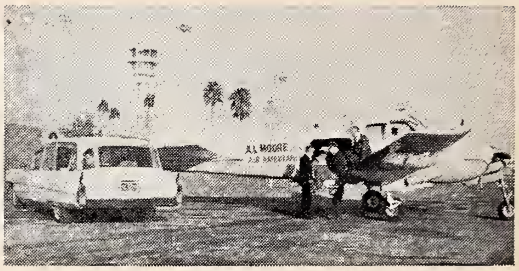

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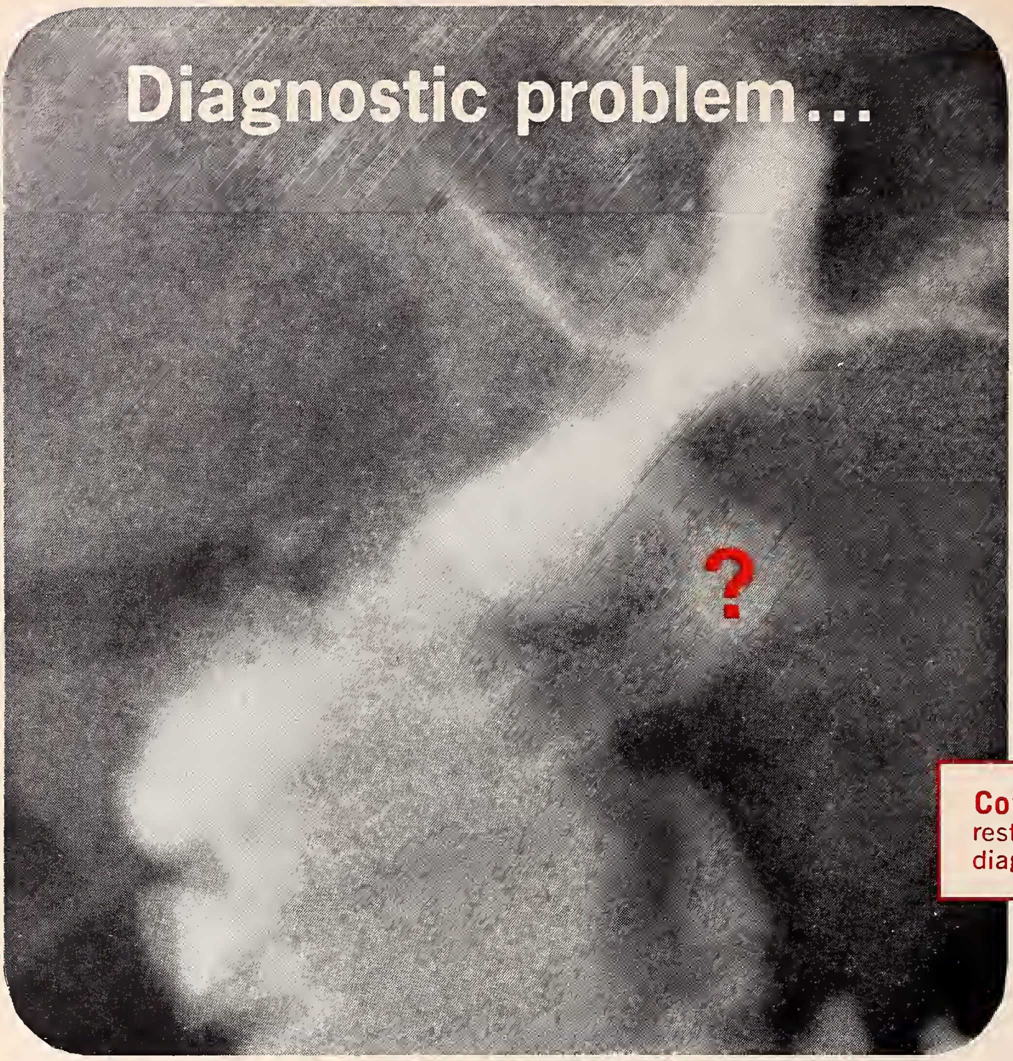
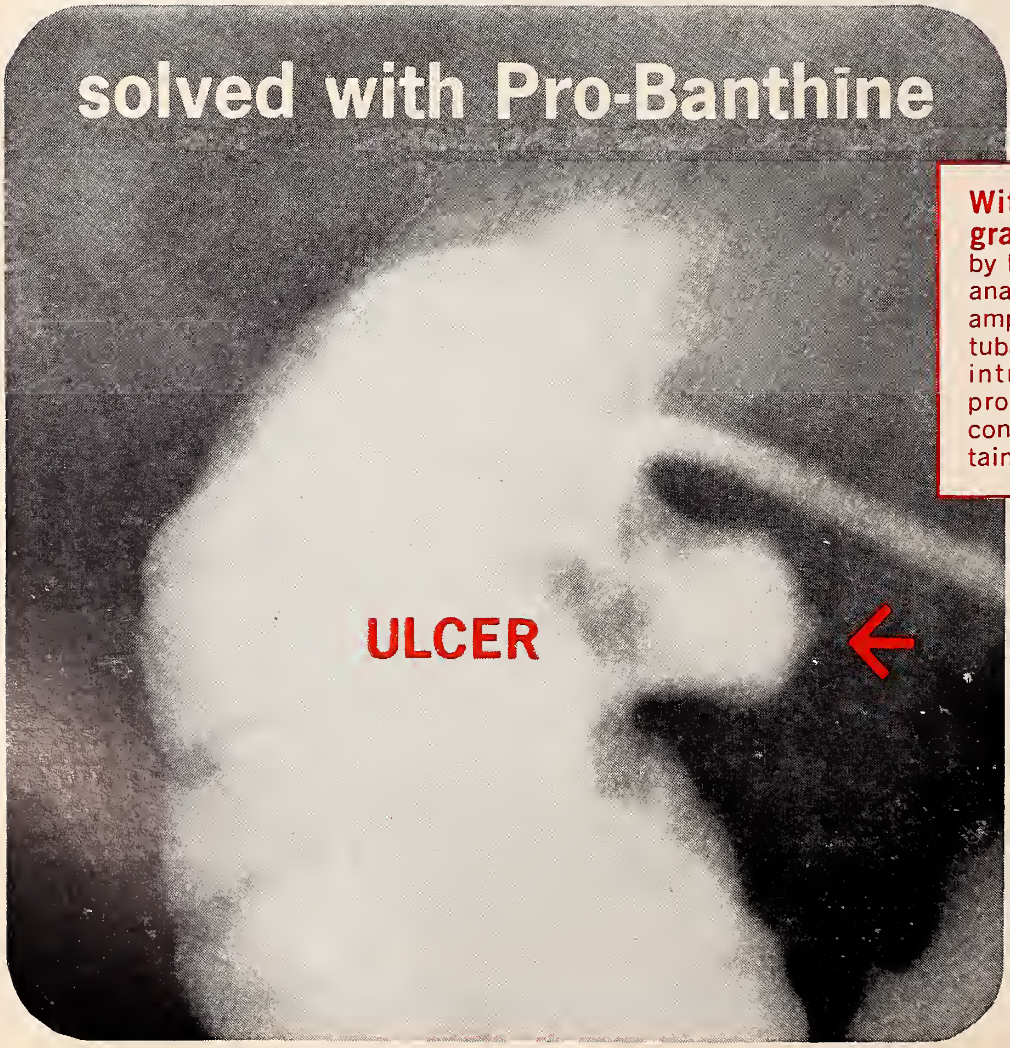


Conventional x-rays of the restless duodenum are often diagnostically indefinite.



With hypotonic duodenography duodenal calm induced by Pro-Banthīne permits clear anatomic appraisal. In this example the duodenum was intubated. Pro-Banthīne, 60 mg. intramuscularly, produced prompt aperistalsis. Double contrast visualization was obtained with barium and air.

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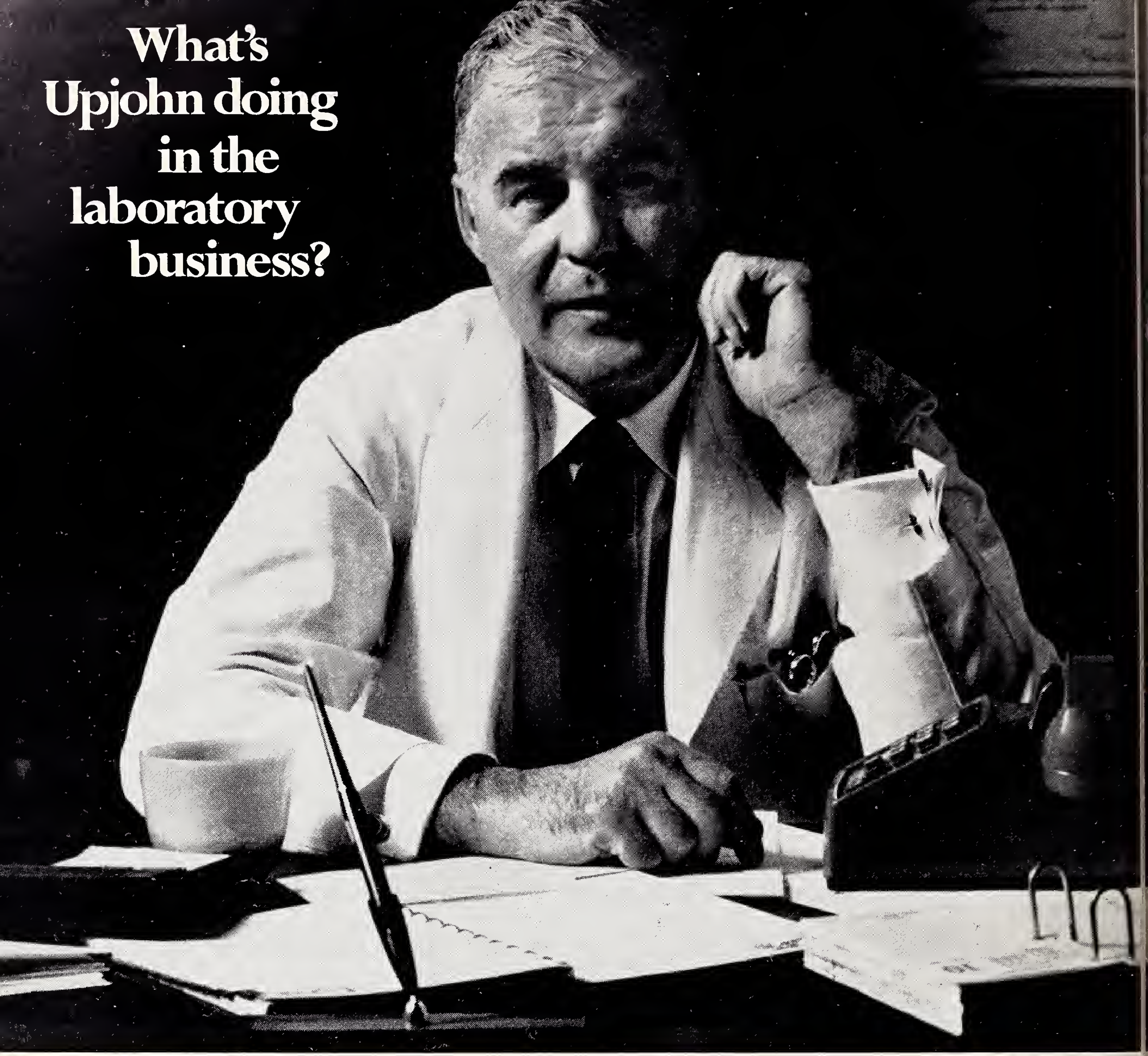
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Literature on indications and dosage available on request.

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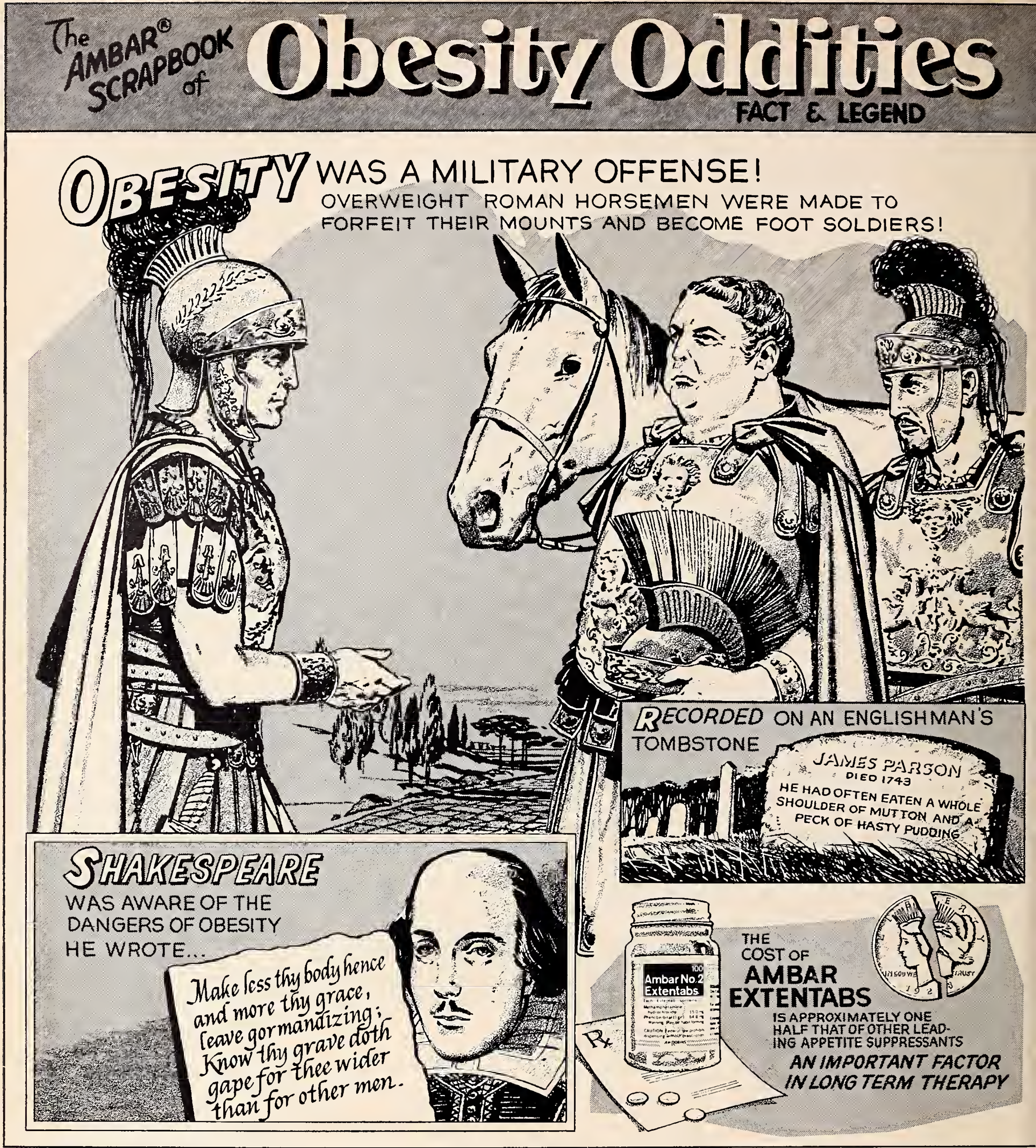
References:

(1) Siver, R. H.: CMD, *21*:109, September 1954. (2) Frykman, H. H.: Minn. Med., *38*:19-27, January 1955. (3) McGivney, J.: Tex. State Jour. Med., *51*:16-18, January 1955. (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., *15*:15-16, October 1965. (5) Weekes, D. J.: N.Y. State Jour. Med., *58*:2672-2673, August 1958. (6) Weekes, D. J.: EENT Digest, *25*:47-59, December 1963. (7) Abbott, P. L.: Jour. Oral Surg., Anes., & Hosp. Dental Serv., 310-312, July 1961. (8) Rapoport, L. and Levine, W. I.: Oral Surg., Oral Med. & Oral Path., *20*:591-593, November 1965.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NOVEMBER, 1969/VOL. 26, NO. 11

ARIZONA MEDICINE

THE WESTERN JOURNAL OF MEDICINE

JOURNAL OF ARIZONA MEDICAL ASSOCIATION • MEDICAL SOCIETY OF THE UNITED STATES AND MEXICO

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Published monthly by The Arizona Medical Association, Inc., with offices at 4601 N. Scottsdale Rd., Suite 201, Scottsdale, Arizona 85251. Subscription $5 a year, single copy 50 cents. Second class postage paid at Scottsdale, Arizona, and at additional mailing offices.

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THE WESTERN JOURNAL OF MEDICINE,

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THE BREAKUP of a business partnership, the crack-up of a marriage, the shake-up of being fired or reduced to bankruptcy…after any significant loss or severe blow to sel esteem, *both* anxiety and depression almost always follow.

FOR MODERATE TO SEVERE ANXIETY WITH COEXISTING DEPRESSION

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TRANQUILIZER-ANTIDEPRESSANT

Containing perphenazine and amitriptyline HCl

For prescribing information, including indications, contraindications, warnings, precautions, and side effects, please see following page.

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INDICATIONS: Patients with moderate to severe anxiety and/or agitation and depressed mood; patients with depression in whom anxiety and/or agitation are severe; patients with depression and anxiety in association with chronic physical disease; schizophrenics with associated depressive symptoms.

CONTRAINDICATIONS: Central nervous system depression from drugs (barbiturates, alcohol, narcotics, analgesics, antihistamines); bone marrow depression; urinary retention; pregnancy; glaucoma. Do not give in combination with MAOI drugs because of possible potentiation that may even cause death. Allow at least 2 weeks between therapies. In such patients therapy with TRIAVIL should be initiated cautiously, with gradual increase in the dosage required to obtain a satisfactory response.

WARNINGS: Patients should be warned against driving a car or operating machinery or apparatus requiring alert attention, and that response to alcohol may be potentiated.

PRECAUTIONS: Suicide is always a possibility in mental depression and may remain until significant remission occurs. Supervise patients closely in case they may require hospitalization or concomitant electroshock therapy. Untoward reactions have been reported after the combined use of antidepressant agents having various modes of activity. Accordingly, consider possibility of potentiation in combined use of antidepressants. Not recommended for use in children. Mania or hypomania may be precipitated in manic-depressives (perphenazine in TRIAVIL seems to reduce likelihood of this effect). If hypotension develops, epinephrine should not be employed, as its action is blocked and partially reversed by perphenazine. Caution patients about errors of judgment due to change in mood.

SIDE EFFECTS: Similar to those reported with either constituent alone.

Perphenazine: Should not be used indiscriminately. Use caution in patients with history of convulsive disorders or severe reactions to other phenothiazines. Likelihood of untoward actions greater with high doses. Closely supervise with any dosage. Side effects may be any of those reported with phenothiazine drugs: blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia); liver damage (jaundice, biliary stasis); extrapyramidal symptoms (opisthotonos, oculogyric crisis, hyperreflexia, dystonia, akathisia, dyskinesia, parkinsonism) usually controlled by the concomitant use of effective antiparkinsonian drugs and/or by reduction in dosage, but sometimes persist after discontinuation of the phenothiazine; severe acute hypotension (of particular concern in patients with mitral insufficiency or pheochromocytoma); skin disorders (photosensitivity, itching, erythema, urticaria, eczema, up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions); peripheral edema; reversed epinephrine effect; endocrine disturbances (lactation, galactorrhea, disturbances of menstrual cycle); grand mal convulsions; cerebral edema; altered cerebrospinal fluid proteins; polyphagia; paradoxical excitement; photophobia; skin pigmentation; failure of ejaculation; EKG abnormalities (quinidine-like effect); reactivation of psychotic processes; catatonic-like states; autonomic reactions such as dryness of the mouth, headache, nausea, vomiting, constipation, obstipation, urinary frequency, blurred vision, nasal congestion, and a change in the pulse rate; hypnotic effects; pigmentary retinopathy; corneal and lenticular pigmentation; occasional lassitude; muscle weakness; mild insomnia; significant unexplained rise in body temperature may suggest intolerance to perphenazine, in which case discontinue. Antiemetic effect may obscure signs of toxicity due to overdosage of other drugs or make diagnosis of other disorders such as brain tumors or intestinal obstruction difficult. May potentiate central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol), atropine, heat, and phosphorous insecticides.

Amitriptyline: Careful observation of all patients recommended. Side effects include drowsiness (may occur within the first few days of therapy); dizziness; nausea; excitement; hypotension; fainting; fine tremor; jitteriness; weakness; headache; heartburn; anorexia; increased perspiration; incoordination; allergic-type reactions manifested by skin rash, swelling of face and tongue, itching; numbness and tingling of limbs, including peripheral neuropathy; activation of latent schizophrenia (however, the perphenazine content may prevent this reaction in some cases); epileptiform seizures in chronic schizophrenics; temporary confusion, disturbed concentration, or transient visual hallucinations on high doses; evidence of anticholinergic activity, such as tachycardia, dryness of mouth, blurring of vision, urinary retention, constipation, paralytic ileus; agranulocytosis; jaundice. The antidepressant activity may be evident within 3 or 4 days or may take as long as 30 days to develop adequately, and lack of response sometimes occurs. Response to medication will vary according to severity as well as type of depression present. Elderly patients and adolescents can often be managed on lower dosage levels.

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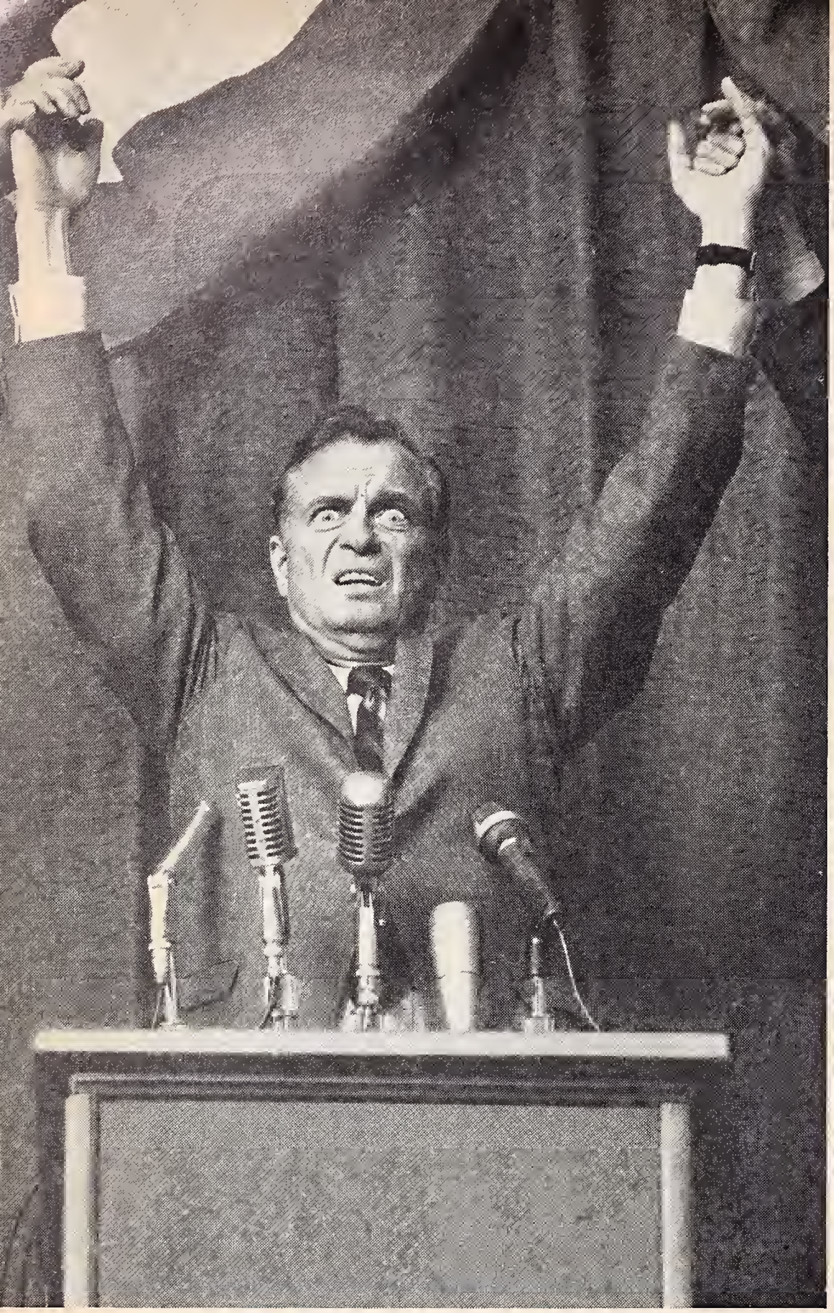
BOB

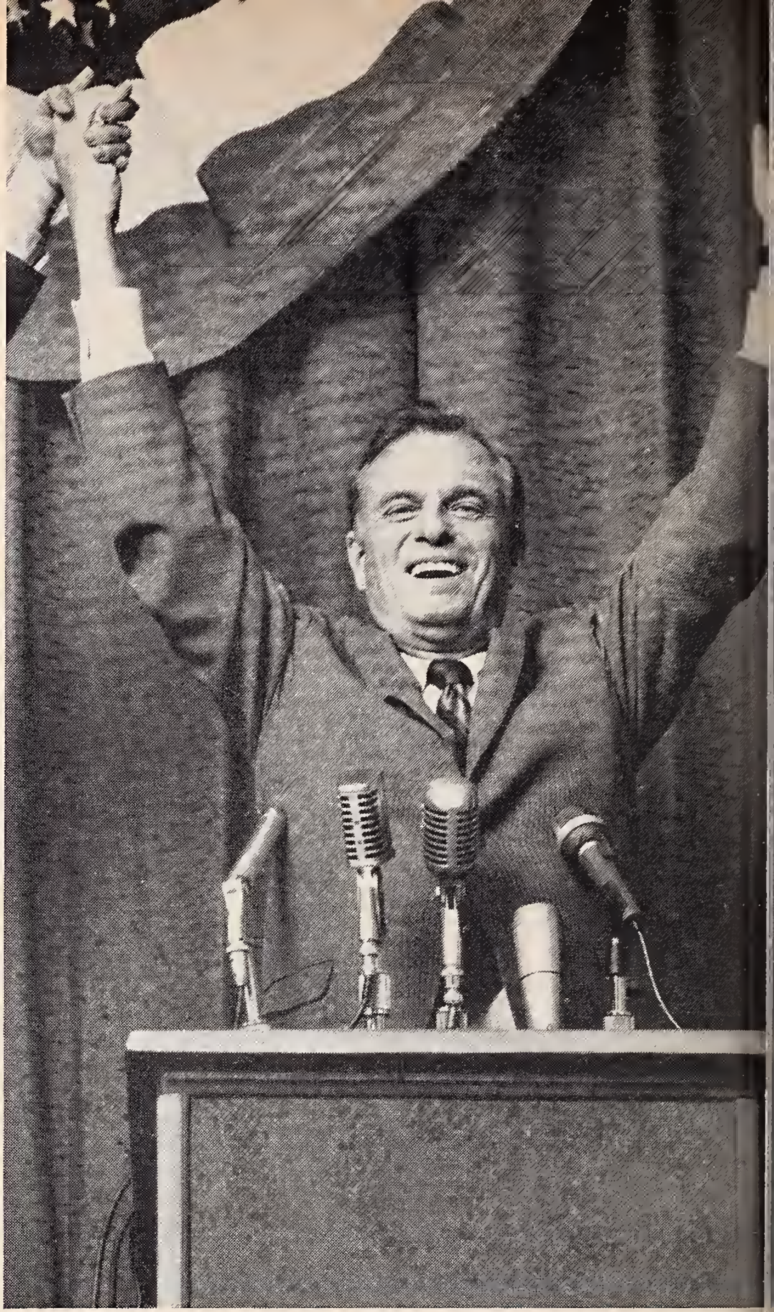
This issue of *Arizona Medicine* is one of the most interesting we have published, and the first one to include a regional journal insert. However, its true significance lies not in these achievements, but rather in its dedication to our retiring Executive Secretary, Bob Carpenter.

When your editor wrote to men who knew Bob well, advising them of the plans for a special issue ,the response was immediate. Their remarks which appear this month are varied in length and style. But through them all run the same delicate threads, weaving a human tapestry of admiration, understanding, and appreciation that portrays Bob Carpenter's dedication to the challenge of guiding "his doctors" through twenty years of growth and change.

I wrote to only a few, but had I written to one hundred there would have been one hundred similar tributes. For their words of praise reflect the appreciation of all Arizona physicians who want to thank him for his constancy of purpose and devotion, to thank him for his tireless energy and gracious sense of values, but most of all to thank him for being Bob Carpenter.

Robert F. Lorenzen, M.D.
Editor





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References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis o Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth J. L. A., *et al.*: Gastroenterology *44*:146 1963. 4. Berman, H. H., *et al.*: Dis. Nerv Syst. *25*:430, 1964. 5. Friend, D. G.: Clin Pharmacol. Ther. *5*:871, 1964.

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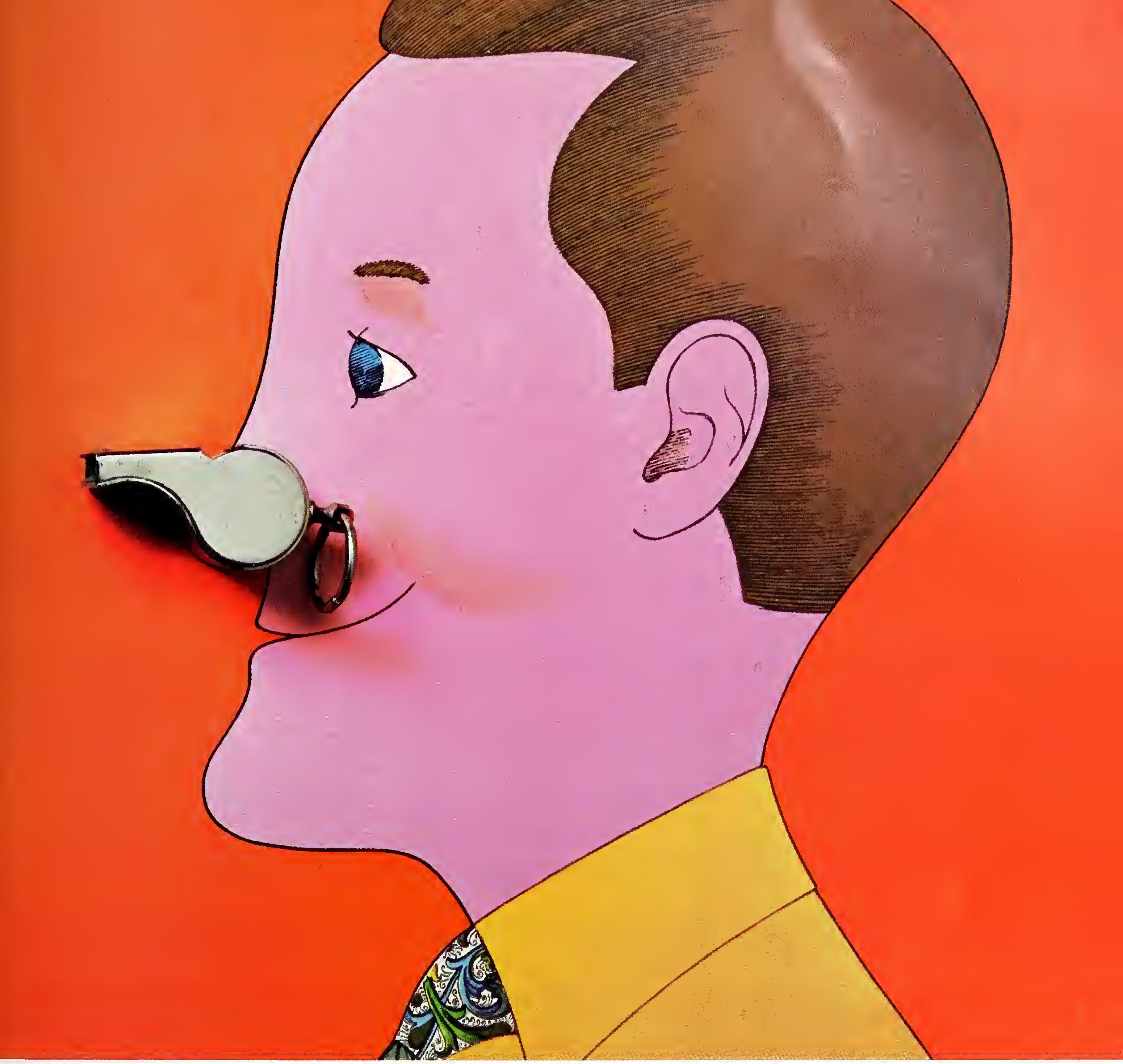

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Precautions: Until patient's response has been determined, he should be cautioned against engaging in operations requiring alertness. Administer with care to patients with cardiac or peripheral vascular diseases or hypertension.
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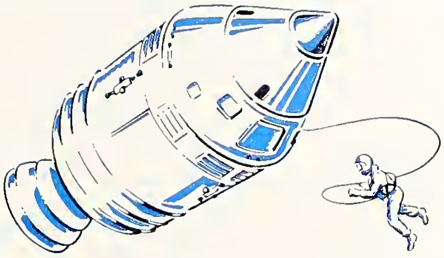
The compound analgesic that calms instead of caffeinates

Indications: Phenaphen with Codeine provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.



Man in space, now fait accompli, re-emphasizes the importance of Uro-Phosphate therapy. Research into the effect of space travel on the astronaut reveals that weightlessness causes loss of bone calcium. As the bones are required to bear less and less of the weight of the body they lose calcium, increasing the calcium content of the urine. When physical activity is reduced, the acidity of the urine should be adjusted to keep increased calcium in solution . . . . a prophylaxis to prevent kidney or bladder calculi.

Uro-Phosphate®

NOW A SUGAR-COATED TABLET

Each tablet contains: METHENAMINE, *300 mg.;* SODIUM ACID PHOSPHATE, *500 mg.*

Uro-Phosphate gives comfort and protection when inactivity causes discomfort in the urinary function. It keeps calcium in solution, preventing calculi; it maintains clear, acid, sterile urine; it encourages complete voiding and lessens frequency when residual urine is present.

Dosage:

For protection of the inactive patient 1 or 2 tablets every 4 to 6 hours is usually sufficient to keep the urine clear, acid and sterile.

2 tablets on retiring will keep residual urine acid and sterile, contributing to comfort and rest.

A clinical supply will be sent to physicians and hospitals on request.

Uro-Phosphate contains sodium acid phosphate, a natural urinary acidifier. This component is fortified with methenamine which is inert until it reaches the acid urinary bladder. In this environment it releases a mild antiseptic keeping the urine sterile.

Uro-Phosphate is safe for continuous use. There are no contra-indications other than acidosis. It can be given in sufficient amount to keep the urine clear, acid and sterile. A heavy sugar coating protects its potency.

WILLIAM P. POYTHRESS & COMPANY, INC., RICHMOND, VIRGINIA 23217

Manufacturers of Ethical Pharmaceuticals

No place for beginners

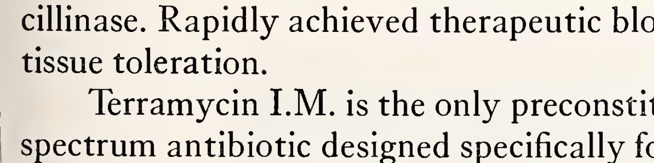
Terramycin®
(oxytetracycline)

Fire victim. Examination reveals second degree burn of lower leg. To combat shock, restore circulatory volume and replace protein loss, plasma is administered. Local pressure dressing applied. Limb elevated to limit the flow of lymph. About 36 hours after admission the patient develops an elevated temperature and complains of pain at the site of the lesion. Dressing removed. A suppurating slough area has developed over part of the burn. A swab specimen is taken for culture and the slough area is debrided. Antibacterial treatment is begun with Terramycin I.M. Days later, recovery is progressing, and the laboratory report shows a mixed infection with a predominance of susceptible coliform bacteria, confirming the therapeutic choice. Terramycin therapy is continued until all signs of infection disappear.

Experience has shown that Terramycin offers special advantages in treating bacterial infections complicating burns, when strains of causative organisms are susceptible. Broad-spectrum antibacterial coverage. Activity unaffected by penicillinase. Rapidly achieved therapeutic blood levels. Proven tissue toleration.

Terramycin I.M. is the only preconstituted broad-spectrum antibiotic designed specifically for intramuscular use. Requires no refrigeration. Remains stable for at least two years. Available for immediate use in Isoject,® a disposable injection unit. In difficult as well as routine cases, when tests reveal susceptible organisms, consider Terramycin. One of the world's most widely used broad-spectrums.

Terramycin® I.M.
(oxytetracycline)



Pfizer LABORATORIES DIVISION
New York, N.Y. 10017

Contraindicated: In individuals hypersensitive to any of the components of this drug.
Warnings: If renal impairment exists, even usual doses may lead to excessive systemic accumulation and possible liver toxicity. In such patients, lower than usual doses are indicated and for prolonged therapy oxytetracycline serum level determinations may be advisable.
Terramycin may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans.
Use of oxytetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of teeth. This effect occurs mostly during long-term use of the drug, but it has also been observed in usual short-treatment courses.
During treatment with tetracyclines, individuals susceptible to photodynamic reactions should avoid direct sunlight. Discontinue therapy at first evidence of skin discomfort.
Note: With oxytetracycline, phototoxicity is not believed to occur and photoallergy is very rare.
Precautions: Use of broad-spectrum antibiotics occasionally may result in overgrowth of nonsusceptible organisms. Where such infections occur, discontinue oxytetracycline and institute specific therapy.
As with all intramuscular preparations, Terramycin Intramuscular Solution should be injected well within the body of a relatively large muscle. *Adults:* The preferred sites are the upper outer quadrant of the buttock (i.e., gluteus maximus), or the mid-lateral thigh. *Children:* It is recommended that intramuscular injections be given preferably in the mid-lateral muscles of the thigh. In infants and small children the periphery of the upper outer quadrant of the gluteal region should be used only when necessary, such as in burn patients, in order to minimize the possibility of damage to the sciatic nerve.
The deltoid area should be used only if well developed such as in certain adults and older children, and then only with caution to avoid radial nerve injury. Intramuscular injections should not be made into the lower and mid-thirds of the upper arm. As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel.
Increased intracranial pressure with bulging fontanelles has been observed occasionally in infants receiving therapeutic doses of the drug, but such signs and symptoms have disappeared rapidly on cessation of treatment with no sequelae.
Adverse Reactions: Subcutaneous and fat-layer injection may produce mild pain and induration which may be relieved by an ice pack. Very mild gastrointestinal disturbances, not requiring discontinuance of the drug, may occur occasionally. Allergic reactions, including anaphylaxis, rarely have been observed.
Dosage: *Adult:* The optimal dosage varies, depending on the type and severity of infection. Unless otherwise specified, a dose of 100 mg. every 8 to 12 hours, or a single daily dose of 250 mg. should be adequate for the treatment of most mild or moderately severe infections. In severe infections, 100 mg. every 6 to 8 hours, or 250 mg. every 12 hours may be necessary.
Serum levels obtained by the recommended dosages are comparable to those provided by the oral dosage of 1 to 2 Gm. daily in adults. Antibiotic therapy should be continued for at least 24 to 48 hours after all symptoms and fever have subsided.
In certain diseases specific courses of therapy may be recommended as a general guide. In primary and secondary syphilis for example, the daily administration of 2 Gm. oxytetracycline, orally, in divided doses for two weeks has given good results. In cases of gonococcal infection two intramuscular injections of 250 mg. each, or one intramuscular injection of 250 mg. combined with one gram given orally as a single dose, will usually suffice, but repetition of this therapy will be required in an occasional case.
In the treatment of hemolytic streptococcal infections, therapy should continue for at least 10 days to prevent development of rheumatic fever or glomerulonephritis. In the treatment of staphylococcal infections indicated surgical procedures should be carried out in all cases.
Pediatric: A dosage of 3 mg./lb./day in two doses has been found satisfactory in the treatment of most mild to moderately severe infections. For more severe infections, higher dosages may be indicated and should be adjusted accordingly.
Terramycin Intramuscular Solution provides maximum absorption and patient toleration with minimal local irritation.
Supply: Terramycin (oxytetracycline) Intramuscular Solution: available in single dose, prescored glass ampules containing 100 or 250 mg. oxytetracycline/2 cc., Isoject® syringes containing 100 or 250 mg. oxytetracycline/2 cc. and 10 cc. multiple dose vials containing 50 mg. oxytetracycline/cc.
More detailed professional information available on request.

Appearances may be deceiving

It may be tetracycline

but it's not ACHROMYCIN® V
Tetracycline HCl

unless it bears this signature.

250 mg. and 100 mg. capsules

Contraindications: Hypersensitivity to tetracyclines. *Warning:* In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs. *Precautions:* Nonsusceptible organisms may overgrow; treat superinfection appropriately. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood). *Side Effects: Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

Upon adverse reaction, stop medication and treat appropriately.

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BOARD OF DIRECTORS

Meeting of the Board of Directors of The Arizona Medical Association, Inc., held in the Convention Center of the Safari Hotel, Scottsdale, Arizona, Sunday, September 14, 1969, convened at 10:10 a.m., James L. Grobe, M.D., Vice President and Chairman, presiding.

WELCOME

A quorum being present, the meeting was called to order by Dr. Grobe, invocation by Dr. Wagner, and a cordial welcome extended by the Chairman to all guests in attendance. The Chairman introduced Gerald L. Barnett, who will join the staff as Associate Executive Director, Tuesday next.

MINUTES

Approved minutes of the meeting of the Board of Directors of this Association held July 27, 1969.

ArMPAC BOARD OF DIRECTORS

Dr. Kahle reported upon the total membership to date and financial status of the ArMPAC organization. Effort is continuing toward the selection of an appropriate speaker for the forthcoming annual banquet.

It has been and will continue to be the policy of the Chairman to make recommendations for appointment or reappointment to membership on the ArMPAC Board of Directors without commitment, the ArMA Board of Directors to make the final decision. It is necessary to make certain contacts to determine individual availability and willingness to serve, but without commitment. Two vacancies on the ArMPAC Board continue to exist. Recommendations from the ArMA Board would be most welcome.

REPORT ACCEPTED.

BENEVOLENT AND LOAN FUND COMMITTEE

Scholarship Awards

The Benevolent and Loan Fund Committee reported the following 1969-70 Scholarship Awards of $500.00 each (TOTALING $11,000.00):

1. Beauchamp, Robert Frederick (Phoenix)
2. Breiman, Richard Spencer (Tucson)
3. Dahl, Steven I. (Mesa)
4. Federschneider, Jerome M. (Tucson)
5. Hooper, III Edward Young (Casa Grande)
6. Maciulla, Gregory James (Tucson)
7. Manning, Michael Rollin (Tucson)
8. McBride, Cris Dewaine (Tucson)
9. Nudo, Richard Anthony (Phoenix)
10. Poliakoff, Raymond Marion (Tucson)
11. Qualls, Susan Patricia (Tucson)
12. Reineberg, Edward Jere (Eloy)
13. Roach, Mary Julia (Phoenix)
14. Ruben, David Alan (Tucson)
15. Schold, Jr., Stanley Clifford (Phoenix)
16. Soulliard, Mary Carol (Tucson)
17. Chick, Russell Paul (Scottsdale)
18. Freestone, Steven Wilford (Mesa)
19. Goggin, Daniel Anthony (Carefree)
20. Wasem, Donald Ben (Phoenix)
21. Youngkin, Tyler (Phoenix)
22. Bedard, Charles Kent

Approved scholarship awards by the Benevolent and Loan Fund Committee to twenty-two (22) qualified first-year medical students of $500.00 each, totaling $11,000.00; also, two (2) similar awards previously made totaling an additional $1,000.00. The surplus scholarship fund at the beginning of the year (Account 303) totaled $14,157.32, leaving a balance of $2,157.32.

Resolution Amendment

Approved introduction of a resolution in the House of Delegates of this Association in annual meeting next amending the second Resolve of Resolution 14-64 to read as follows:

RESOLVED, that the Benevolent and Loan Fund Committee be directed to institute and proceed with a scholarship grant for any resident of Arizona who is attending as a freshman, his or her first year in an approved medical school; this scholarship to amount to a Five Hundred Dollar Scholarship from the Arizona Medical Association; and

Operational Review

Dr. Cloud, Chairman of the Benevolent and Loan Fund Committee, reviewed the operation and policies of that body pursued through the years associate with the scholarship award program, its requirements and guidelines. A meeting is generally held in August of each year to review applications in hand and determine eligibility. The medical students have had outstanding scholastic achievements and demonstrated need, so much so that available funds have permitted recognition of each to date. Only one applicant in the past has disqualified himself because of the Arizona residency requirement and possibly on no more than two or three occasions has financial need been questionable. The twenty-two awards reported is the highest number so far. Each year the number of applicants increases. As a matter of fact, since the recent awards, eighteen additional applications have been received and are being processed for review. The potential growth of first year medical students will continue upward.

With the growth prognostication, the financial picture becomes even more concerning. Available funds for scholarship purposes have been derived from the interest of reserve savings accounts. Before or after the end of this year such reserves may not be available, the outcome of the building program.

It was suggested that the Committee review this operation in the light of present circumstances and submit recommendations regarding the establishment of new priorities and criteria. As regards the eighteen additional applicants who have filed and any others who might similarly file this year, it appears that consideration will have to be given on the basis of available funds.

BOARD OF MEDICAL EXAMINERS — STATE OF ARIZONA

Licenses

The Board of Medical Examiners of the State of Arizona reported revocations and cancellation of licenses to practice medicine and surgery in the State of Arizona account non-payment of annual license renewal fee; also, reinstatement of license which had been previously suspended. RECEIVED FOR INFORMATION.

Medicine & Surgery Act — Amendment

With regard to work being done at Sage Memorial Hospital in Ganado, now being administered by Project Hope, a charitable organization created for the purpose of providing medical care in under-developed areas, overseas as well as in this country, Otto L. Bendheim, M.D., President of the Arizona Board of Medical Examiners, as an individual, proposes that the Medicine and Surgery Act of this State be amended to waive the statutory fee of $50.00 for temporary licensure for those physicians who spend from one to three months at Ganado or similar institutions. Discussion ensued.

Determined that this suggestion be received for information.

EXECUTIVE COMMITTEE

Financial Report

Accepted the report of the Treasurer covering the month of August, 1969. "Income" $2,169.00 (total Income received — 1969 to date $214,696.06), reflecting an "under-budget" of $45,928.94 (1969 Budget $260,625.00). "Expenditures" $15,387.40 (total Expenditures — 1969 to date $156,853.94), reflecting an "under-budget" of $108,643.56 (1969 Budget $265,497.50, as amended). REPORT ACCEPTED.

1969 Budget of Appropriations — Reductions

Adopted the following recommended appropriation reductions affecting the 1969 Budget:

501	SALARIES	$5,500.00
502	PAYROLL TAXES	500.00
524	FURNITURE & FIXTURES EXPENSE	1,900.00
500i	HISTORY & OBITUARIES EXPENSE	200.00
500p	PROFESSIONAL	5,000.00
500r	PUBLIC RELATIONS	7,000.00
500y	GOVERNMENTAL SERVICES	4,000.00

Lease Agreement

Authorized execution of a lease agreement, prepared by counsel, to be entered into with the Board of Medical Examiners of the State of Arizona for "leased premises" to be located in the new ArMA building at 810 West Bethany Home Road, Phoenix, Arizona, for the term of one year at a monthly rental of $394.16 commencing the first day of January, 1970, and on the first day of each month thereafter to and including the first day of November, 1970; and $394.24 on the first day of December, 1970 (total $4,730.00).

LEGISLATIVE COMMITTEE

Doctor Henderson reported that arrangements were progressing satisfactorily for the scheduled dinner-meeting to be held at the Cloud Club, Phoenix, October 2, 1969, at 7:00 p.m. Arizona legislators, principally those comprising the Public Health and Welfare Committees of the Senate and House, have been invited to meet with the members of the Legislative Committees of both this Association and Maricopa County Medical Society, and ArMA staff, for the purpose of becoming better acquainted in an endeavor to develop mutual understanding and good will. REPORT RECEIVED.

PROFESSIONAL COMMITTEE

Approved the appointment of Robert C. Evans, M.D. (Scottsdale) as a member of the Professional Committee for the term 1969-72 to serve as Chairman of the Section on Medicine and Religion. Dr. Wagner expressed the hope Dr. Evans will accept the assignment.

He read the content of his letter forwarded by him, as Chairman of the Professional Committee, to his Section chairmen, setting forth certain guidelines to be followed in the reroganization of the activities of this committee. REPORT RECEIVED.

COMMUNICATIONS

Hospital Expansion Monopoly — Corporate Practice of Medicine

Reported acceptance of assignment by all members appointed by the Board of Directors, July 27, 1969, to serve as an Ad Hoc Committee to Study the Practice of Medicine by Hospital Corporations. RECEIVED FOR INFORMATION.

OTHER BUSINESS

ArMA Insurance Programs

Dr. Flynn expressed his views regarding actions taken at the last Board of Directors meeting, especially relating to the professional liability insurance program underwritten by the Hawaiian Insurance and Guaranty Company, Ltd., Charles Fisher, broker of record. Considerable discussion ensued.

It was determined that this Board of Directors reaffirm the designation of Charles Fisher as broker of record for professional liability insurance; further, that this entire matter be referred back to the Medical Economics Committee for re-review, evaluation and recommendaiton.

Locum Tenens Council

Approved the appointments of Drs. Boyden L. Crouch (Phoenix), representing Maricopa; William R. Engvall (Winslow), President Navajo; Francis Findlay (San Manuel), President Pinal; Raymond E. Hammer (Kingman), President Mohave; Thomas B. Jarvis (Globe), President Gila; Dermont W. Melick, Chairman (Tucson); David D. Smith (Flagstaff), President Coconino; Manus R. Spanier (Prescott), President Yavapai; and James Volpe, Jr. (Yuma), representing Yuma, to serve as members of the Locum Tenens Council suggested by the Board of Directors, July 27, 1969. Responses from the Presidents of the County Medical Societies of Apache, Cochise, Graham, Greenlee, Pima, and Santa Cruz are being awaited.

Blue Shield Feasibility Study — Use of Computer

Dr. Grobe called the Board of Directors' attention to the proposed feasibility study in the more effective use of the computer tying in the doctor's office, the hospital, and Blue Cross-Blue Shield. Such study is estimated to cost approximately $30,000.00, and will be considered by the Blue Shield Board next Saturday for approval or disapproval. REPORT RECEIVED.

AMA Clinical Convention — Denver

Authorized attendance to the AMA Clinical Convention, Denver, Colorado, November 30 to and including December 3, 1969, at Association expense, to include the Delegates (2); the Alternate Delegates (2); the President-Elect; the corporate Secretary; the Executive Director and the Assistant Executive Director.

Waiver of Building Assessment

Fred L. Patterson, Jr., M.D. (Sierra Vista), Active member of Cochise County Medical Society and this Association, requested and was granted a waiver for one year of his 1969 Building Assessment payment ($15.00), account illness.

Truth in Lending — Resolution — AMA

The following resolution relating to "Truth in Lending" (Consumer Credit Protection Act), prepared by counsel, proposed for introduction in the House of Delegates of the American Medical Association in Clinical Convention scheduled to be held in Denver, Colorado, November 30 through December 3, 1969, was approved for such introduction, subject first to its referral to AMA for review and favorable comment as to content authenticity:

WHEREAS, it is unethical for physicians to add service charges or interest to their patients' accounts; and

WHEREAS, Section 103(f) of the Consumer Credit Protection Act, 15 U.S.C.A. § 1601 (1968), defines a creditor as one who extends credit "for which the payment of a finance charge is required"; and

WHEREAS, the Consumer Credit Protection Act was therefore not intended to apply to physicians who do not require the payment of any finance charges; and

WHEREAS, Regulation Z, 12 C.F.R., § 226 (1969) promulgated by the Board of Governors of of the Federal Reserve Board, may nevertheless subject physicians not imposing any finance charges to the requirements of the Consumer Credit Protection Act; and

WHEREAS, Regulation Z thus places a burden on physicians which is not consistent with the purposes of the Consumer Credit Protection Act and which requires unnecessary paper work of physicians; therefore be it

RESOLVED, that the full resources of the American Medical Association be devoted to establishing that the Consumer Credit Act does not apply to physicians who do not require the payment of finance charges; and be it further

RESOLVED, that a report on progress made in this regard shall be made to this House of Delegates at the next Annual Convention of the American Medical Association.

Articles of Incorporation and Bylaws Committee

Dr. Henderson, Chairman of the Articles of Incorporation and Bylaws Committee, urged the members of the Board of Directors to give consideration to need for any amendments to the Bylaws of the Association and submit such suggestions to the committee now for its consideration. This will afford ample time for preparation of necessary resolutions in advance of the next annual meeting of the ArMA House of Delegates. REPORT RECEIVED.

MD-DO Meeting

It was reported by Bruce Robinson that plans are being developed for a meeting between the Executive Committee of this Association and a committee of the Arizona Osteopathic Medical Association, as previously directed, tentatively set for October 26, 1969, to be held in Casa Grande. The agenda will include such subjects as:

1. The roles of each organization in providing continuing medical education for all physicians in Arizona.
2. Cooperative efforts in the area of legislative activities.
3. Hospital staff privileges
   a. Provision of courtesy and consultation privileges
   b. Full staff privileges

REPORT RECEIVED.

Headquarters Building Progress

It was reported by Bruce Robinson that the headquarters building project is currently twenty-one days behind schedule because of difficulty on the part of the contractor to procure adequate skilled labor. The completion date thereby has been advanced to November twenty-fifth. REPORT RECEIVED.

Neighborhood Doctors' Office

Dr. Dudley called attention to an article appearing in American Medical News, September 8, 1969 issue, entitled: "Physicians Aid Poor in Phoenix Program." A new program has been established in Phoenix called Neighborhood Doctors' Office directed toward those who are either too "wealthy" for state or county aid, and because of age do not qualify for a federal program. With the aid of two local hospitals, physicians' offices were set up on the southeast and southwest sides of Phoenix. Local physicians volunteer their time to serve in these offices. Patients from a specified geographical area come to one of the two offices where they receive the type of care they would normally have in a private physician's office. The only difference is that the fee they pay is only a percentage of the physician's regular office fee. The cooperating hospitals, St. Luke and Memorial, also have agreed to accept this percentage as full payment for daily, drug, laboratory and other expenses. Dr. Augusto Ortiz is one of several physicians participating in the program mentioned in the article.

It was determined to forward a letter of commendation to Dr. Ortiz and others participating in the Neighborhood Doctors' Office program, congratulating them and thanking them for their efforts in this direction.

U of A College of Medicine

The chairman expressed the appreciation of the Board of Directors for the attendance at this meeting of Dr. DuVal, Dean of the University of Arizona College of Medicine. The Dean submitted to any questions or report desirable referable to progress being made at the College of Medicine. He thanked the Board for the privilege of attendance, advising that he or a member of his staff would make themselves available in the future for similar purpose, if desirable.

Blue Cross-Blue Shield

Mr. Foster, Executive Director, Arizona Blue Cross-Blue Shield, was invited to offer any comment he might wish to make regarding operations of Blue Cross-Blue Shield and expressed his appreciation for the privilege of attendance.

MEETING ADJOURNED AT 12:20 P.M.

Edward Sattenspiel, M.D.
Secretary

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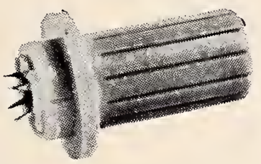

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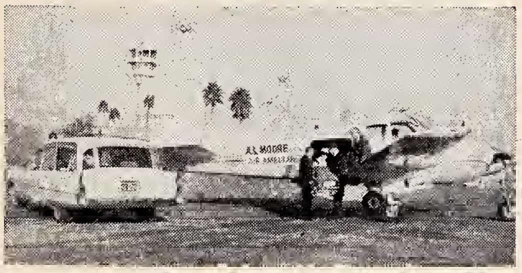

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Material submitted for publication in ARIZONA MEDICINE should conform to the following policies:

1. Manuscripts, including references or bibliography, should be typewritten, double-spaced, on one side of the paper only, and the original and a carbon enclosed.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.
3. Although the Editors try to catch inaccuracies, the ultimate responsibility is the author's.
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Original Articles

SURVEY OF STROKE PATIENTS

Mary Opal Wolanin, R.N.

Albert G. Wagner, M.D.

As the result of a survey directed to general practitioners and internists, it is estimated that there are approximately 7,000 patients with strokes in the State of Arizona (or 4.15 percent of the population). Of these patients, approximately 2,325 were admitted to hospitals (exclusive of the Veterans Hospitals) with strokes, constituting the principal need for admissions to extended-care units and nursing homes. It is hoped that this study will be of value as part of the Arizona Regional Medical Program in providing ample facilities for the care of these patients.

Introduction

In order to plan realistically for any situation, an estimate of the present and future must be made, presumably on the basis of the past and current events. The Regional Medical Program is challenged to improve the care of patients with Heart Disease, Stroke and Cancer. To improve involves the necessity of assessing the current procedure and resources, comparing with the optimum and using such information to provide planning. The Arizona Regional Medical Program has appointed a Stroke Steering Committee with representation from all the disciplines which are involved in returning the Stroke patient to his potential health state. Lacking was a clear picture of the actual morbidity[1] of Stroke in Arizona, or the incidence[2] for Stroke. This is not a reportable condition and no central registry has been developed for maintaining statistics. Mortality rates are more easily obtained. *Arizona Health Trends,* Mortality 1950-1966[3] shows a steadily rising line on the graph from 61.6 deaths per 100,000 population in 1950 to 67.7 in 1966. Since morbidity and incidence are of primary interest the *Patient Origin Study*[4] was consulted. This study was developed through Blue Cross-Blue Shield, the Hospital Association, Arizona Medical Association, Arizona Osteopathic Association and the Arizona Nursing Home Association, with the Phoenix and Tucson Health Planning Councils. During one month there were 129 discharges from hospitals of patients with diagnosis of Stroke. If this rate stayed level for the twelve-month period, an incidence of 1,548 could be anticipated. This study, however, did not include all the non-federal hospitals or any of the federal hospitals. The age group utilizing Veterans Hospitals includes many in the age groupings where a high incidence of Stroke occurs. This indicates that the estimate of 1,548 was too low. Added to this fact is the knowledge that not all patients are hospitalized with Stroke, since many occur to patients in nursing homes, or in their own homes. The available statistics were insufficient for a planning base.

Investigation of studies which had been made on patients in the United States as a whole revealed that the discharge rate per 1,000 persons in non-federal hospitals was 1.54 for the Stroke patient.

One successful study has been published for a population of 83,500 in Middlesex County, Connecticut.[5] The incidence figures were gathered from physicians' reports, death certificates and hospital reports. The rate was 2.3 per 1,000. When this was adjusted to the younger age distribution of the population of 1950, by Wylie, this became 1.7.[6] A third study in Rochester, Minnesota, resulted in an estimate of 4.2 per 1,000 population.[7]

A fourth study based on National Health Survey Statistics gives an index of morbidity for Stroke of 3 per 1,000 population in New York, Westchester and Rockland.[8]

Table I.

Index		Incidence of Stroke Based on Population of 1,690,000
Wylie	(1.7)	2,873
Middlesex	(2.3)	3,718
National Health Survey	(3)	5,070
Rochester	(4.2)	7,098

Comparison of estimated incidence of Stroke in Arizona in 1968, using the four indices.

This wide discrepancy could result in totally different estimates in a large population. In Arizona, using the Valley National Bank's approximation of the 1968 population as 1,690,000 results in the above varying estimates for the incidence of Stroke in Arizona.

Such comparison highlights the problem. What is the actual and true incidence? How many Stroke patients are under the care of Arizona's practitioners?

Methodology

It was decided that only a survey of the Arizona Stroke patients would give a clue as to the dimensions of the problem. The first step was to devise a survey which would yield the greatest amount of information with the least effort by the participants. It was decided that certain groups of physicians would probably care for the majority of Stroke patients, and although the patients were referred to other physicians in specialty areas, the management would remain with the family physician. The general practitioner and internist see Stroke patients initially and follow them throughout the course of illness, so the neurologist and vascular surgeon were not included in the sample. The Arizona section of the *American Medical Directory, 24th Edition, 1967, Part II*, and *Directory of the Arizona Osteopathic Physicians, 1968*, were used to establish a list of physicians.

A simple straightforward letter stating the problem accompanied a simple questionnaire on a return addressed postcard. Questions were followed by blocks in which a number could be written. County was identified in one corner and the physician was asked to check if he were a general practitioner, internist or other. The present case load of Stroke patients was asked, in addition to a six-month estimate of patients in hospitals, nursing homes or at home. Some physicians added another category, showing that they saw the patient in the office. This made the category "home" of dubious value, for it was

Table II.

COUNTY	Medical Practitioners[a]	Osteopathic Physicians[b]	Average Case Load per Practitioner[c]	Total CVA Case Load of Respondents	Extrapolation to Total Practitioner Population[d]	Deaths[1]	Hospital Discharg
Apache	10		3.5	7	35	8	1
Cochise	27		5.1	56	137	43	48
Coconino	26		8.4	143	218	20	12
Gila	8		10.4	52	83	18	36
Graham	5		21.6	108	135	18	48
Greenlee	5	1				9	36
Maricopa	387	100	9.3	1,968	4,417	582	852
Mohave	9		3.7	15	33	11	24
Navajo	8		8	55	64	30	
Pima	110	42	7.4	617	1,021	222	331
Pinal	34		6.9	119	238	38	48
Santa Cruz	7		7.3	23	51	7	36
Yavapai	25		5	53	125	49	48
Yuma	20		11.25	135	225	40	60
Totals	681	143	8.6	3,351	6,772	1,095	1,580

a. General practitioners and internists were selected from **American Medical Directory**, 24th Edition, 1967, Part II, published by the American Medical Association.

b. Compiled from the listings of general practitioners and internists of the **Arizona Osteopathic Medical Asociation 1968 Directory**, 5057 East Thomas Road, Phoenix.

c. The average case load per practitioner was obtained by dividing the reported case load of reporting physicians in each county by the number of physicians reporting.

d. Extrapolated figure was obtained by multiplying average case load per practitioner by the known number of practitioners in county.

1. **Vital Statistics Annual Report**, 1966, Arizona State Department of Health. (Latest statistics available.) Table 36, p. 31.

2. **Patient Origin Study.** Analysis of discharges from 63 Arizona hospitals during the month of March, 1967, Arizona State Department of Health, pp. 111-113.

not interpreted the same by each respondent. The letter asked for an estimate, rather than a search through the files.

The first replies were received two days after the mailing, with a peak reached a week later; however, replies were returned for five weeks.

Findings

The response from physicians was a surprising 59%, which is much higher than expected in a survey of this type. Many physicians had taken the time and trouble to write in additional information that they felt might be of value. A surprising number signed their names. Table II gives the overall response on the part of physicians in each county. The number of patients given by the physicians from a county was averaged and extrapolated to the total physician population for the entire county, giving an estimate of the total Stroke population. The average per practitioner was quite high in some of the outlying counties of the state, and ranged from a maximum of 21.6 in Graham County to 3.7 in Mohave County, with an average case load for the Arizona physician of 8.6 patients. Table II gives the estimated number of Stroke patients in each county as the result of this survey.

Although the effort was made, obtaining statistics from the Veterans Administration was not successful. The final statistics then do not include data from the Veterans Hospitals and outpatient departments. Based on the data collected, the number of Stroke patients in Arizona is 6,772. It may safely be assumed that the Veterans Administration, which has many patients in the age group where Stroke is most prevalent, would change this number to 7,000, if not more. On the basis of 7,000 patients with Stroke, it may be assumed that the index which applies to Arizona is closer to the Rochester figure of 4.2. Arizona, with 7,000 patients in 1,690,000 population has an index of 4.15.

Of special interest was the total of 959 patients listed as cared for in nursing homes. This study represents a 59% response; it must be assumed that the actual number is proportionately higher. This is confirmed by the Arizona Blue Cross, with its Medicare figures. The principal diagnosis for admission to the extended care units and nursing homes is for Stroke.[9] The hospitalized Stroke patients reported were 1,860 by 59% of the physicians. If this is extrapolated to the total physician population, it becomes 2,325 hospital admissions for Stroke (exclusive of Veterans Hospitals). This exceeds by 777 the estimate (1,548) given in the *Patient Origin Study.*[10] Since that study was based on less than a complete sample of the non-profit hospitals, and on none of the government hospitals, the discrepancy would seem valid.

Conclusions

Indices of themselves are valueless unless they assist with making estimates on which to base sound planning. It is believed that this survey has resulted in a realistic figure on which to plan Stroke programs for the state. In addition, it has given a basis for determining where the Stroke patients are.

As a quantitative device only, it leaves many questions unanswered. One would ask what degree of impairment and disability is present in the 7,000 patients. It would be useful to know qualitative details. In any survey, there is a reasonable tolerance that one can expect from the respondent. The more detailed the information required, the greater the sample loss. In this instance, it was decided to focus on quantitative information only in order to obtain a high response. This was achieved.

Gratitude is expressed to those busy physicians who took the time to answer the questionnaire and contribute to these findings. The paucity and variance of previous studies leads the writers to the belief that although this is a very simple study, it also is one of the few, and may help to confirm the Rochester study as the more dependable index of the incidence of Stroke in this country.

1. Morbidity: the sick rate, the ratio of sick to well members of a community.
2. An expression of the rate at which a certain event occurs.
3. **Arizona Health Trends,** Mortality 1950-1966, Table 6, p. 12.
4. **Patient Origin Study.** An analysis of 19,144 discharges from 63 Arizona hospitals during Harch, 1967, Arizona State Department of Health, July 1967.
5. Eisenberg, H., et al. "Cerebrovascular Accident Incidence and Survival Rates in a Defined Population, Meddlesex County, Connecticut," **Journal of American Medical Association,** 189:883-8, September 21, 1964.
6. Wylie, Charles M., "Hospital Care for Patients with Stroke in the Acute Stage," **Journal of the American Medical Association,** 193:10::135.
7. Fields, William S., and William A. Spencer. **Stroke Rehabilitation; Basic Concepts and Research Trends,** St. Louis, Mo.: Warren A. Green, 1967, p. 14 and Table IV.
8. Cugliano, Anna and Peter Marano, **Heart, Cancer, Stroke and Related Diseases,** a Data Book, New York Regional Medical Program, December 1968, p. 41.
9. Personal phone conversation with Mr. Don Yost of Blue Cross/Blue Shield on September 9, 1968. The principal disease categories found in nursing homes fall in this order:
    1. Cerebral hemorrhage.
    2. Fracture of the neck of the femur.
    3. Coronary and associated heart diseases. General heart disease.
    4. Pulmonary disease.
    5. Diabetes.
    6. Cataracts.
    7. Arterial disease.
10. **Patient Origin Study,** Op. Cit.

PESTICIDE INTOXICATIONS IN ARIZONA

C. J. Harris, M.D. **S. R. Kemberling, M.D.**

E. A. Williford, M.D. **D. P. Morgan, M.D.***

Poisonings by pesticides, though infrequent, are of importance, particularly in agricultural areas. Three cases of acute poisoning from insecticides are reported here, one with a fatal termination. Toxicology and therapy are briefly discussed.

Intoxications by pesticides represent only a very small fraction of the total reported poisonings in Arizona. In agricultural areas, however, unreported intoxications undoubtedly occur with some regularity, and the prevalence of household pesticides constitutes a continuing threat to small children. The success of treatment is determined by the dose and nature of the poisoning agent, by the promptness with which unabsorbed poison is removed, and by the appropriate use of antidotes.

The dependence of agriculture on a wide variety of potent insecticides is not likely to change in the near future. Currently, long-term ecologic considerations are forcing abandonment of the persistent chlorinated hydrocarbons in favor of the degradable but much more acutely toxic organophosphates. Termite and household pest control still rely heavily on chlorinated cyclodienes and cyclohexane, but a number of "low toxicity" organophosphates, and carbamates are gaining popularity. Thus, exposure of the public to an assortment of new chemicals is currently substantial, and is unlikely to diminish in the foreseeable future.

Acute poisonings usually fit either of three categories: 1) occupational, 2) home accidents, or 3) suicides. Presented here are reviews of Arizona cases representing each type, followed by some retrospective comment.

Case #1

About 6:00 a.m., September 9, 1968 a 19-year-old loader of agricultural aircraft was sprayed by a mixture of methyl and ethyl parathion from a leaking pump. He did not decontaminate himself for at least 30 minutes, "due to the urgency of the application schedule." He continued to work and may have had some subsequent exposure to the same or similar chemicals. He did not report symptoms until about 10:00 a.m. the following morning. Complaining that he felt ill, he was advised by the superintendent to take the day off. He drove home unattended, collapsing from weakness on arrival. He was intensely nauseous, weak, and diaphoretic but apparently never lost consciousness. Due to some confusion on the part of his relatives he was not hospitalized for about two hours after arriving home. At the emergency room, his plasma showed no cholinesterase activity, and RBC cholinesterase was reduced to 28% of normal. This specimen contained 38 ppb of ethyl parathion and 19 ppb of methyl parathion, measured by gas-liquid chromatography (GLC).

He was treated with serial injections of Atropine, first 5 mgm then 2 mgm, intravenously, 25 minutes apart. Clinical improvement was prompt. Despite catheterization and intravenous fluids, he remained anuric the first 20 hours of hospitalization. Fortunately, increased fluid infusion prompted very adequate urine flow thereafter. Moderate concentrations of paranitrophenol (a degradation product of parathion, with some irritant effect on the urinary tract) were found in the urine. No glucose, amino acid nitrogen or albumin were excreted.

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*Epidemiologist, University of Arizona Community Studies Pesticide Project, supported by Contract No. 86-64-84 with the Division of Community Studies, Office of Product Safety, Bureau of Medicine, Food and Drug Administration, Consumer Protection and Environmental Health Service, Public Health Service, Department of Health, Education and Welfare, Atlanta, Georgia.

A test of renal tubular phosphate reabsorptive function[6] done 18 days after poisoning showed a definitely depressed value of 76%. When repeated four months after poisoning, phosphate reabsorption had risen to 88%.

A series of hematologic and enzymatic tests failed to show any other residual abnormalities resulting from the intoxication. Clinical recovery was apparently prompt and complete.

Comment:

Vigorous efforts by private physicians and public health personnel in the 1950's and early 1960's[12] reduced an alarming initial incidence of organophosphate poisonings to the present minimal level. It seems probable that industrial intoxications could be eliminated almost entirely by certain modifications in packaging and handling procedures, if not by strict enforcement of standard safety techniques. Nearly all recent poisonings have occurred in new employees, often hired only for the duration of a busy spray season. Intensive briefing and supervision of these personnel are now the most pressing requirements in the interest of their safety. In the past, routine cholinesterase testing has contributed a measure of protection in detecting faulty handling of chemicals, and perhaps in warning those chronically exposed of excessive cumulative dosage. Routine testing, however, offers no protection from occasional inadvertent heavy contamination by accident or carelessness.

Diagnosis of organophosphate poisoning is not always easy on the basis of symptomatology and clinical signs alone.[13] Serum and red cell cholinesterase tests are very helpful in confirming suspected cases, although pitfalls have to be borne in mind. Certain agents, particularly carbamates, have relatively little effect on the blood enzymes. Also there is extreme variation in individual susceptibilities to organophosphate compounds. Interpretation of the test is aided greatly by availability of a pre-exposure control value for comparison.[27] Firms engaged in the handling of these chemicals are urged to secure blood cholinesterase values on their employees prior to exposure.

Treatment depends, in part, on the severity of intoxication.[13] In severe poisonings, relief of airway obstruction and adequate artificial respiration are the first essentials. Complete decontamination is always mandatory. Atropine must be given parenterally in dosage (usually 2-5 mgm q 10-30 minutes) adequate to achieve and maintain full atropinization until the toxicant is metabolized. This is often adequate management. In severe poisonings, pralidoxime (Protopam, 2-PAM) one gram, given slowly intravenously, reverses the chemical bond between toxicant and enzyme, and therefore offers more definitive treatment. There is no contraindication to the simultaneous use of pralidoxime and Atropine.

The incidence of serious sequelae from organophosphate poisonings is not accurately known. Serious CNS damage has apparently occurred in at least one parathion poisoning case.[25] Malathion was strongly suspected of causing peripheral neuropathy in two persons who applied it over a long period of time, although in one case DDT may have played a part.[20] From time to time, we hear of cases of marked personality change following organophosphate poisoning. Renal tubular defects may occur,[6] but apparently resolve in a matter of weeks or months.[18]

Case #2

About noontime November 12, 1968, a 3-year-old white male was brought to Tucson Medical Center by his mother. He had convulsed about 30 minutes previously. His mother thought he had swallowed some tablets about 9:30 a.m., which she identified tentatively as aspirin. In the E. R., he convulsed mildly a second time, showing myoclonic movements of the extremeties. He was disoriented and confused, being unable to identify his mother.

The child was not febrile. Pallor was prominent. Blood pressure and pulse were not remarkable. The neck was supple. Pupils were equal, neither constricted nor dilated. Superficial and deep tendon reflexes were very hyperactive.

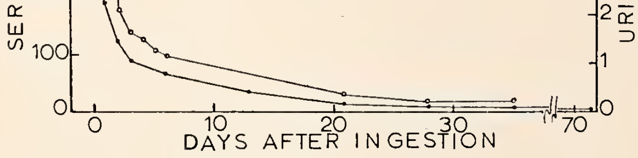
Thorough gastric lavage yielded no identifiable tablet residues. Blood salicylate level was 5 mgm%; barbiturates were not found in the blood. On questioning the boy's playmates, it was determined that he had swallowed tablets spilled from a trash can in the back yard. The mother believed these were insecticide. Analysis of the gastric contents by gas-liquid chromatography identified the toxicant as lindane, a pesticide commonly sold in tablet form for use in an electric vaporizer. Lindane concentration in the patient's blood was 468 parts per billion, in the urine 7.7 ppb.

No further seizures occurred, but disorientation persisted. The boy vomited three times during the afternoon. About 8:00 p.m., he aroused from the confusional state, as though recovering from a general anesthetic. He took and retained food and water.

On the third hospital day, the tip of the liver was palpable. Nine SGOT values measured during the five weeks after lindane ingestion ranged from 43 to 84 units. At 10 weeks, the SGOT read 30 units. In all other respects, recovery progressed without incident. Serial blood cell counts gave no indication of bone marrow injury, and urinalyses showed no more than an occasional trace of albumin and a rare hyaline cast. There were no indications of residual CNS damage.

Urinary excretion of lindane proceeded essentially as though dependent on the store of chemical remaining in the body. (Figure 1.) U/P concentration ratios suggest a clearance of about 10-25 ml serum per day. The appearance of several unidentified peaks on the urine chromatogram indicated that chemical conversion to various metabolites had probably occurred, accounting for a substantial fraction of the total excretion.

FIGURE 1
TIME COURSE OF
SERUM AND URINE LINDANE
CONCENTRATIONS FOLLOWING INGESTION



Comment:

Lindane (the γ isomer of hexachlorocyclohexane*) is representative of the persistent chlorinated hydrocarbon insecticides currently very popular in household pest control. It is available to the public in various forms, one being a tablet for thermal volatilization. In Europe, lindane candles are widely used.[28] From time to time, both tablets and candles appeal to children.

Symptoms and signs of acute poisoning are remarkably uniform:[8, 23, 26, 28] 1) cerebral disturbances, ranging from mild confusion to coma, 2) myoclonic seizures (simulating grand mal) lasting a few minutes to several hours, 3) pallor or cyanosis, the latter depending on the severity of seizures. EKG changes[5] and signs of liver injury[2, 14] have been noted. Despite the initial grave manifestations, prognosis is generally good: of eighteen poisoning cases in children reported or mentioned in the foreign literature,[2, 8, 11, 23, 28] two were fatal. Both of the latter involved overwhelming dosages. Extreme exposures have also caused adult deaths,[2, 5] but less severe poisonings usually resolve favorably.[19]

Serious sequelae from prolonged heavy exposure have been reported, one child suffering optic atrophy and spastic paraplegia.[5] Three others in the same poisoning epidemic showed temporary depression of the red count and hemoglobin, apparently due to bone marrow injury. The author remarks that the effects of lindane itself may have been amplified by severe malnutrition and intestinal parasitism in these victims. Partly because lindane is made by the chlorination of benzene, bone marrow damage has been expected in lindane intoxications. However, the end product is a fully saturated ring, and bone marrow injury has not been prominent in the acute toxicological picture.

An important point in treatment is the adverse effect of giving absorbable fats or oils (including milk, cream, butter, etc.).[28] Lipids capable of dissolving chlorinated hydrocarbons enhance the chemical's toxicity many fold, no doubt by expediting transport to the body tissues. Thorough gastric lavage, activated charcoal, and later saline catharsis, are all of value. Barbiturates are indicated only for the control of propracted, life threatening seizures.

Case #3

A 45-year-old white woman was found unconscious by her husband when he returned home in the early evening of July 1, 1968. Having been alone since noon, she could have been ill or unconscious as long as six hours. On arrival at the emergency room, measures were taken to reverse total cardiac and respiratory arrest. Positive pressure ventilation via endotracheal tube was necessary for two hours before any voluntary respiratory activity appeared, and voluntary respiratory effort continued to be inadequate throughout most of the hospital course. Circulatory function was restored by external cardiac massage and intravenous levarterenol (Levophed). Maintenance of adequate blood pressure remained dependent on this pressor agent the following 36 hours.

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*Popularly, but incorrectly, known as "benzene hexachloride."

On admission the patient was totally unconscious and areflexic. No involuntary motor activity was evident, although seizures did develop about 8 hours later. Some mucous about the mouth was seen by the husband at home, but no salivation or frothy sputum was observed thereafter. Pupils were of intermediate size and unreactive to light. There was no diaphoresis, diarrhea, or retching. She had not been incontinent. Moderate bradycardia without gross arrhythmia, was noted.

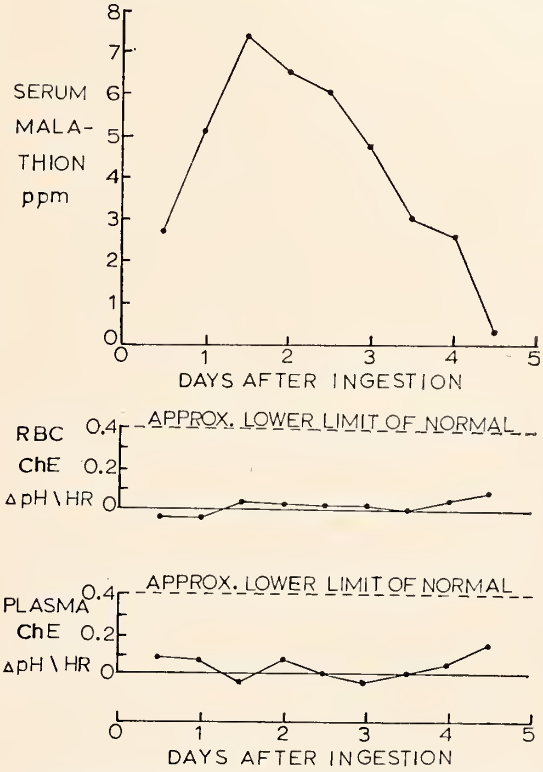
The urine showed 4+ glycosuria and blood sugar was 210 mgm%. However, serum acetone was negative, and blood acid-base measures pointed to severe respiratory acidosis superimposed on moderate metabolic acidosis. Repeat blood sugars were all in the normal range. Serum calcium was 7.4 mgm%, potassium 2.3 mEq/L, sodium 166 mEq/L, salicylate 15 mgms%, barbiturates negative.

A disagreeable odor about the patient was noted by the family and several examiners. Although identification was uncertain, some type of organophosphate poisoning was strongly suspected. Malathion was kept at home, but none appeared to be missing from available supplies. Nevertheless, thorough gastric lavage was carried out, and 4 mgm Atropine were given IV.

By morning, relatives had discovered at home a drinking glass containing residues of Malathion. GLC analysis showed large quantities of the chemical in the gastric washings, and the serum level measured 2.67 parts per million. Cholinesterase activity was absent from red cells and plasma. Pralidoxime, (2-PAM), 1 Gm IV, was given, and repeated q 12 to 24 hours the succeeding four days. Atropine 2 mgm IV was administered, and a dose of 1-2 mgm IV or IM was given every 1-4 hours the succeeding four days.

On July 3, the patient showed slight voluntary movement and responded momentarily. Pupils were dilated. An enema was administered. The endotracheal tube was removed in view of stronger respiratory effort. However, ventricular fibrillation occurred four hours later, requiring difibrillation, external cardiac massage, and reintubation of the trachea. Thereafter, the patient remained completely comatose, and again required levarterenol to maintain blood pressure. Laboratory studies this date showed elevated serum SGOT (135) and LDH (240). Blood malathion level reached 7.4 ppm, much increased over the previous day (Figure 2).

FIGURE 2
SERUM MALATHION CONCENTRATIONS
AND BLOOD CHOLINESTERASE ACTIVITIES
FIVE DAYS FOLLOWING INGESTION



Tracheostomy was done the following day. Clinical status remained the same.

Spinal tap on July 5 showed 636 crenated RBC/cu. mm., but no other abnormalities. Generalized edema appeared, which responded partially to mannitrol diuresis the next 48 hours. However, indications of pneumonitis became prominent, and progressed despite antibiotic therapy, intensive tracheobronchial hygiene, and assisted respiration. The patient expired in circulatory failure 5½ days following ingestion of Malathion.

Autopsy revealed generalized edema, including severe pulmonary edema, and bronchopneumonia. A small recent subdural hematoma was found, with no associated abnormalities to suggest head trauma.

Comment:

The "muscarinic" symptomatology typical of organophosphate poisoning (miosis, salivation, diarrhea, bradycardia) was absent in this case. In fact, the early suspicion of Malathion poisoning was based on the foul odor emanating from the patient. To titrate the dosage of Atropine, it was necessary to rely on the pulse rate, recorded by the cardiac monitor.

Exceptional clinical manifestations, not readily accounted for in terms of cholinesterase inhibition, have been noted before in Malathion poisoning.[13] In the present case, massive dosage and protracted absorption of Malathion, made inevitable by the long interval between ingestion and lavage, may have played a part. One may postulate a counteracting adrenergic action of the pesticide (and a central sympathetic effect has been suspected[15]) but the necessity for levarterenol in sustaining blood pressure makes this mechanism seem unlikely. Possibly at high dosage levels, Malathion is in some way anticholinergic as well as cholinergic.

Pathologic findings in other fatal Malathion poisonings[9, 16] have included severe grades of venous hyperemia of the viscera and generalized edema. The latter was very prominent in the present case. A direct action of Malathion on capillary integrity is certainly suggested, and may account for the subdural hematoma noted at autopsy.

The major intercurrent complications to be expected are: 1) Pneumonitis[1, 4, 10] secondary to pulmonary edema, copious bronchial secretions, and respiratory paralysis, 2) encephalopathy, manifest as coma, psychotic behavior, and/or seizures,[1, 4, 25] and 3) myocardial irritability, with ventricular fibrillation. The latter was prominent in the present case, and marked irritability was seen by another author, who used intravenous Lidocaine successfully to control ventricular tachycardia.[4]

The value of pralidoxime, and even of Atropine, in treatment is not so clearcut in the case of Malathion as in other organophosphate poisonings. In a single case, pralidoxime seemed to have an adverse effect.[22] Atropine has no effect on the "nicotinic" actions[24] of organophosphates (i.e. muscle weakness and tremors) which are particularly prominent in Malathion poisoning.

Removal of unabsorbed poison from the gut once it has passed the pylorus is problematic. Catharsis may spread a bolus of toxicant over a large absorptive area, leading to greatly increased absorption. Laboratory evidence has shown activated charcoal to be of value in experimental poisonings in animals.[21] However, in vitro studies suggest that very large quantities of charcoal would have to be mixed intimately with the toxicant to achieve substantial binding of a large dose.[7] If charcoal is used, it must be given well in advance of the laxative, to avoid inactivation of the charcoal by the medication.

Suicidal attempts using organophosphates, and particularly Malathion, are becoming a significant statistic in locations as far flung as Hungary,[9] Australia,[25] and British Guiana,[17] no doubt reflecting the wider availability of the insecticide. Contrary to the impression one might get from its extensive household usage, and high LD50 (1100 mgm/Kg in the rat), death has become a very common result of Malathion ingestion.[9, 16, 25]

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President's Page

WHAT DOES ArMA DO FOR ME?

OR

DO ALL MY DUES GO FOR A PLUSH BUILDING FOR THE OFFICE STAFF?

A better question, perhaps, is "What *should* a state association do for an individual doctor?" My answer to this question would be, directly "Very little." But the State Association should do, and we hope it does, a service to the doctors of Arizona and their patients. If our goal is the best possible medical care for the people of Arizona, how does the State Association further this ideal? There is a need for more physicians in Arizona. The Association has loans available to the students, and we have given out 27 scholarships to freshman medical students this year. The Medical Practice Act was liberalized some two years ago primarily because of the active interest and support of your organization. We would like to take a little credit for the formation of the medical school in Arizona. Our annual meeting in 1959 under Dr. Melick's guidance was devoted to the proposition of a medical school in Arizona and from this came a lot of the drive to accomplish this goal. There is an active recruitment program to interest high school and college students in the health field. This is aided by literature from AMA but primarily done by the local physicians. We publish a journal each month with scientific articles and other news of interest to Arizona physicians.

Medical Memos helps you keep abreast of medical problems and hopefully give you some help in discussion of these problems with your non-medical friends.

Health Tips are sent to the schools every Monday to interest students and teachers in health matters. In legislative matters we hope to kill the bad bills and pass the good ones. This is an area where the individual cannot function nearly as effectively as the state organization. As a state organization we work with the different insurance groups particularly CHAMPUS, the Industrial Commission and Medicare in an attempt to get more equitable fees and reasonable rules and regulations. More than 360 members of your association serve on the 46 committees making recommendations to the Board to make your lot an easier one. We have a dedicated staff working under the Executive Director.

These people do the day by day chores of the association, assist with the committees, and the Board of Directors. As you watch these people, you realize they work long hours. Committee members see them at night and on Sundays in the committee meetings, but I see them the next morning in the office doing their regular job without worry about overtime pay. The Annual Scientific Meeting is the largest scientific medical meeting in the state. Over 42 papers were given at the last meeting and this year promises to be even better. Yes, but what has ArMA done for me recently? Well, we built a new building . . . . . .

Richard O. Flynn, M.D.
President

Dean's Page

HEALTH, MEDICAL CARE, AND ECOLOGY

Health professionals today increasingly recognize the impact of the environment on individual and community health. Formerly, health research concentrated on the model of patient illness rather than on disease prevention, but we now realize that comprehensive health care is much more than treatment of symptoms. It includes the primary prevention of disease, consideration of those environmental aspects of disease which affect the individual and his family, and, beyond clinical treatment, a more positive promotion of health. Community and individual health, therefore, are ecological.

Over the past half century, the major contributions to the increase in life expectancy were improvements in nutrition, housing and sanitation. Indeed, the major component was the reduction of infant mortality, to which improved nutrition and sanitation have probably contributed more than any other factors. However, specific medical care now has much more to offer than ever before. Professor Lawrence Henderson of Harvard University said in 1912, "The random patient with a random disease seeing a random physician has a fifty-fifty chance of benefiting by the encounter." Today the odds are much better, and medical care delivery is currently a major public issue. Yet it may not improve significantly unless we solve the ecological problems of pollution, transportation, housing, nutrition, noise, etc.

In the past, outstanding individual physicians went into the community to help improve living and working conditions. For decades, however, our universities have had little relationship with the communities surrounding them. Almost typically, our medical schools are located in communities afflicted with the most serious urban blight. We learned medicine within an ivory tower, which separated us from a teeming population whose living conditions were conducive to the causation of preventable diseases. Now, universities are looking into the community for research purposes and they are learning that they cannot use the community as a laboratory without becoming involved in community affairs. One medical school in a large eastern urban area recently experienced a difficult confrontation with the community when it set out to build new facilities which would have dislocated thousands of community residents. The school learned that planning without community participation could be disastrous. Fortunately, it came to terms with the community and both will benefit as a result.

Similarly, some medical schools are developing medical care delivery systems in disadvantaged areas where medical care is deficient and health status is low. Incidentally, their programs for training disadvantaged people in new skills may be as important as the development of new medical care delivery systems.

At the University of Arizona, the Department of Community Medicine is developing a Neighborhood Health Center in a blighted urban area which is also the focus of efforts by the city of Tucson for improvement under the Model Cities Act of the U.S. Department of Housing and Urban Development. This facility is intended to be a model for teaching and research. Medical student experience will no longer be limited to the traditional teaching hospital specialty clinics and wards. Students will be oriented toward the patient, his family, and the community. They should be better physicians because of that orientation. Through the Health Center, the Medical School can also contribute toward continuing education of physicians in the community. Physicians may refresh their knowledge by participating in the program and in its conferences and research studies.

A Neighborhood Health Center is by no means the only solution for the health problems of poverty areas, but it will provide a superb opportunity to unite people in medicine with people in the social sciences. The result should be a more equitable distribution of medical care and a concomitant improvement in the ecology of the community.

Monte DuVal

LANDLORD—PART 2

William B. McGrath, M.D.

The commonest cause of death is to feel unwelcome in the world. The poisonous plants, the henbanes and deadly nightshades, the *antagonisms* are out there, beyond the province of medicine. The physician can only harrow the aftermath. It is not by chance that the words, hospital and hospitality, are of the same derivation.

But the roots of psychosomatic disease go deeper yet. They are embedded in the graveyard of philosophy. This is a terrible deficiency, the most critical problem of our time.

All former concepts of ontology and cosmology are fossilized and fit only for listless inspection in a museum of scholarship. Metaphysics has practically been abandoned as unprofitable. Philosophy has served no guardianship in the rash plungings of mass production and materialism. We still sometimes think of God, I suppose, but only as a meaner landlord. The church has become a rent collector for the cheap and crowded rooming house of the world.

People are literally sick of insipid philosophies. When they riot in the streets, they are not throwing up our former values and beliefs; they are retching for want of them.

Everyone expresses a stereotyped alarm: what is the world coming to? This does not have to be just a rhetorical question.

During several generations of warfare and strife we have lost sight of our universal myths. When we do not have communication, conversation, with the supernatural, we are no longer human; we are as vicious as baboons.

Consider, for only one example, the original rites of passage. Individuals did not just grow like weeds. They were cultivated and ultimately harvested as the most important investment of the tribe. For each momentous event in his life, the individual was carefully groomed and made ready. The spirits were invited to participate in his initiation ceremonies, and the rituals were very solemn. There were clearly defined ways in which a person could — and was expected to — merit his passage from one stage or status to the next. And when he claimed his membership, his new identity, there was no question of his welcome.

Sure, we still go through baptisms and graduations and marriages and funerals. But the rites are as threadbare as worn clothing, and almost profane. Judaism split in three, and Christianity fell apart. It is stultifying to have dozens of separate sects when their differences are so trivial. There should be only one religion with a church in every neighborhood.

In a modern environment, so urban and industrial, we still consider the family to be the unit of society, and rightly so. However, one might question whether our emphasis on this point has become too defensive and excluding. Growing up in crowded neighborhoods, children spend a good part of their lives away from home. In a way they should belong to the neighborhood as to a clan. Not just the parents but all the adults, the elders of the tribe, will have to command the young people's respect and assume more responsibility and authority in supervising them. By supervision we do not imply intimidation; we mean a helpful overseeing of their various apprenticeships.

All other creatures are at home in their natural environments. With its certain code of instincts, any wild animal has more free will than man. We are not share-croppers. A paying guest is not a guest, he is a tenant — and this is what we have been trying to get away from.

But a guest is not going to feel welcome unless he knows exactly what is expected of him. This again is why we so desperately need a single and satisfying set of myths, with the rites and rituals to sustain them. Is there any other certificate of admission to society than to observe the rituals, to exercise good manners and morals?

When one is invited to a formal affair, he must wear formal attire. If he doesn't, he will be ostracized or he will make himself an object of derision.

For the civilizing of conduct, primitive people understood that shame is more painful than guilt; ridicule is more effective than punishment. One might take a second look at words like mis-demeanor and dis-grace.

Even ridicule is probably too harsh a term; mirth is more accurate. When a youth breaks the rules of deportment or dress, smokes marijuana or caresses a girl in public or garbs himself in outlandish fashion, we react with angry dismay and with threats and dire predictions. The lad gets the attention he set out to provoke. (It is not just the smiling hysteric who acts hysterically; it is the group around him.) In pre-biblical times a vulgar transgression was dismissed as due to immaturity or ignorance, and it excited no more reinforcing response than giggling and mirth.

It is a harmful knot which binds together our association of crime and punishment. It has not been untied by our failures in human training or by our contrasting success with animals. The error has even resisted our detailed knowledge of conditioned reflexes. The orientation of all authorities — parents and teachers and the law — continues to be automatically and exclusively negative. In any case of wrong behavior we start calling for stricter rules and harsher punishments. So we go on elaborating such intricate systems of penalties that not even a computer could unravel them.

Punishment more often perpetuates bad patterns of conduct than corrects them. If you whip a bucking horse he will only buck the harder. Just once, could not the addict or alcoholic be left alone to sweat it out? Surely ninety per cent of undesirable behavior would extinguish itself, would fall on its face. If it stirred no resistance, if it met only scorn or neglect or indifference.

Actually what we consider punishment often turns out to be reinforcement and disguised reward. A lad who is not willing to attend classes will be expelled from school. A man who refuses to work for an honest living will be put in a penitentiary where he won't have to. Only masochists make threats. Predictable probation for the first offender is an invitation to the first offense. A preposterously long prison sentence, even with its sexual segregation, is hardly suffering to the dull, psychosexually undifferentiated psychopath.

We do subsidize and recompense iniquity. When the prodigal son scoffs at the standards of his family and society, his parents blame themselves and plead for his forgiveness and bribe him not to further misbehave. The decent behavior of the other son is taken for granted, unnoticed and nearly extinguished. If a man is caught in adultery, it is his wife who goes on probation: how did she fail him?

There is no incentive for the accident victim or the injured workman ever to be a good sport, to tolerate a little temporary discomfort and get back to work. Quite the contrary: it is the hysteric or the malingerer who will be compensated.

One of these days, God willing, we'll recall and begin to apply some of the wisdom of our ancestors.

We'll concentrate on finding more positive ways in which to reward good behavior at the expense of bad. Only those who have received traffic citations, for example, will have to renew their driver's licenses. A credit bureau or bank will imprint a special, preferential mark on the card of a man who has not defaulted a debt for five or ten or fifteen years. Business will grant deserved raises and bonuses, but not to everyone or automatically. Unions will encourage a piecework policy, pay for unit accomplishment, and not just for time.

There will be purification rites, too, with fasting and formal ablutions. And they will be like a statute of limitations (say, five years) after which our old reprehensible mistakes will no longer dog our footsteps or ever be mentioned again.

Meanwhile we'll declare a moratorium on science and technology. In this waiting period all religions could someday soon be incorporated into an old-new and more magnificent system. We have climbed up to the roof of the rooming house. It is time for philosophy to call all the faithful to prayer.

BOB CARPENTER: A GREAT TWENTY YEARS

If you take a quiet, meticulous manner, infinite dedication and loyalty, a penetrating, computer-like awareness of the challenge, and flavor these with a quick, jolly smile, a splash of sly wit and a puff of cigar smoke, you have the essence of Bob Carpenter.

For twenty great, exciting years Bob has been the sinewy right arm of Arizona medicine. In those two decades the Arizona Medical Association popped out of its dovecote and grew into a major, vital entity. Bob squired this phenomenon.

I first knew Bob as the affable, somewhat portly gentleman who seemed to be quietly everywhere at the ArMA conventions. You could usually see him perched unobtrusively behind the desk in a front corner of the meeting hall during our House sessions, an ancient, bulging briefcase propped alongside. His neatly combed, straight, gray-black hair, white shirt, somber tie, and unpatterned suit spoke conservatism and propriety. He would studiously jot notes or peer around the room through plain, shell-rimmed bifocals, while chewing a fat cigar. Now and then, when he caught the eye of one of his good doctor friends in the assembly, his intent look would dissolve into a broad grin.

Or you might find him in an outside corridor, tangled in a little caucus of stern-faced, doctor politicians who wanted some sliver of information. It amazed me how he brewed such intense concern with each obscure, tedious detail. Lindsay Beaton once said: "Don't try and look anything up. Ask Bob. He's a goddamn encyclopedia!"

A few years ago ArMA hatched its student loan program and I got to know the inside of Bob. He found himself mixed up in the business of chasing down medical students all around the country (and sometimes out of it) and negotiating raffish, midnight deals with the bank. That moderately hectic adventure in high finance, something new for ArMA, put a miserable chore on his shoulders and favored him with the added burden of a remarkably unknowledgeable committee chairman. At the outset, Bob, I think, although he has never said so to me, did not cotton to the project with reckless enthusiasm. He didn't bitch about the work load it created (the main theme of the loan program was endless clerical detail); yet he was plainly afraid that ArMA had plunged too far. As it turned out, he was nearly right.

Nevertheless, Bob fired up for the job. He arranged a nifty bit of administrative machinery that purred like a finely tuned Rolls Royce. It was provokingly efficient. But no detail escaped, and the program was a smash. It brought acclaim to ArMA and fortune to the bank. Eventually, to Bob's unspoken but obvious delight, AMA-ERF gobbled it up. ArMA got the credit. But Bob Carpenter turned the concept into reality and put guts into the thing. And I learned some of the reasons why Arizona doctors owe him so much.

When I came onto the Board of Directors, I discovered that the Benevolent and Loan Fund Committee wasn't the only outfit doing business with ArMA. There was, of course, the Board itself and its Executive Committee. There were committees for legislative affairs, medical economics, governmental services, to name only three of the big ones. There were all kinds of other standing committees, subcommittees, special committees and ad hoc committees. ArMA had more committees than I had office hours. They pondered through acres of dross, and Bob was their pivot. I think he must have been weaned on a committee.

He was the epitome of Parkinson's Law — in reverse. The more work you threw at him, the more he packed into an hour, and the happier he was. There was no saturation point. His normal business week was seven days, day and night. Asleep, he probably spun his wheels for ArMA.

Most evenings and weekends he was in his office. If you wanted him at 9:00 p.m., the best bet was to call ArMA. By midnight, though, you could usually catch him at home.

"Bob," I would say, in a late call, "What in the world are you doing down there tonight?"

"Well," he might reply in his precise, deliberate way, "I just thought I'd clean up a couple of things while they're fresh in my mind." Then he would puff on the ever present cigar; I could almost hear his brain recycle to my station, like an automatic television tuner. "Now," he would finally say (there was never any use trying to hurry him), "what can I do for you?"

If I had a question, he had the answer. If I had a task, he methodically made of note of what I wanted. And when he quietly announced, ". . . Got it," I knew it was in the bag. He always made me think of the Dictaphone slogan: "It's said, and done."

You would have to love your job to work as hard at it for twenty years as Bob Carpenter did. His idea of fun was to stuff a couple of briefcases full of resolutions and reports and sally off to one of the AMA conventions for a week. Usually he would go a day early, attend a full round of preliminary conferences, then greet the rest of us at sunup the next morning for a breakfast caucus. I don't believe he ever missed a word of any House session, from the first gavel to the last. He also managed to pull the meat out of the important committee hearings. He diligently took notes and stashed myriad scraps of data in the back of his brain. Like too few people, Bob had a panoptic grasp of the broad shape of AMA affairs and the national medical scene.

But for all the tiresome hours of note-taking and speech-listening, Bob really loved the AMA meetings. They were a kind of holiday for him, and he was proud to represent us. He took every chance to say to the folks in New York or Chicago: "My doctors have tripled in number since I came to Arizona." He bragged about our journal, or how we had lobbied through a piece of legislation. Everyone, especially the other state association executives, knew and respected Bob. Plainly a big chunk of Arizona's AMA prestige was his doing.

Certainly the Carpenter humor was a hearty and vital sustenance for Bob during his twenty ArMA years. In fact, in his sly, subtle way, he is one of the funniest men I have ever known.

I remember a couple of years ago when we were returning together from an AMA convention in Chicago. Our big Boeing 727 had just thundered off the runway at O'Hare Field and was climbing westward, destination Phoenix. Bob sat across the aisle from me, comfortably savoring the prospect of a pleasant dinner flight home. The inevitable briefcase full of notes waited at his feet. He reached over and offered me one of those monstrous cigars he loved so much, and chuckled happily at my agonized flinch which this maneuver invariably produced.

Suddenly the plane lurched and perceptibly slowed. Then it heeled over in a steep bank, down and back toward the airport. The no-smoking bell dinged and a nervous bustle spread through the cabin.

In a moment, the captain's firm voice crackled over the loudspeaker. "Please fasten your seat belts," he said, "there's a fire alarm in our number three engine. We're returning to O'Hare for an emergency landing."

One of the stewardesses, a perky little blonde gal whose wide, frightened eyes and set lips made you think she was about to unstring, stopped alongside Bob. He peered up at her with a mischievous twinkle in his eye. His brow furrowed with mock concern. "Oh miss," he said softly, "will there be an extra charge for this landing?"

Bob Carpenter retires from ArMA in December, as much a part of Arizona medicine as any physician ever can be. He is one of the pioneer executive secretaries, that special band of gritty laymen who forsook the world of business and lucre to dare enter the medical fraternity — because the doctors needed that kind of help. Our problems have been the fabric of his life. He has sought our goals, rejoiced with our triumphs, and shared our heartaches.

You can't paint his image with one sweep of a brush, nor can you measure his worth with a simple plaque on the wall or a few polished phrases. You can only say, "Thanks for a great twenty years." For a man like Bob, that's more than enough.

Daniel T. Cloud, M.D.

Robert Carpenter has been at the helm of the Arizona State Medical Association for so many years, that most of us cannot remember the time B.C. (before Carpenter). I'll admit, at first as a member of the Association, I was only vaguely aware he even existed, and for a mighty long time. Then over the many years as an officer of the society, I came to know the real Bob Carpenter, the administrator, the man himself, completely devoted to his job, even to his own personal sacrifice — and that of his family. He wouldn't take a vacation; he wouldn't go home at night; he wouldn't miss a committee meeting. He was always there, working for "my boys." No one could have been more devoted to his work, even when it was often not appreciated by those not close to him. As a result, a good measure of the growth and success of our society lies at his feet. And all of us will benefit because of his helmsmanship and will always be glad we were one of "his boys."

Pubilius Syrus some 40 years B.C. (before Christ) said, "Anyone can hold the helm when the sea is calm." And we have weathered many a storm in the past 20 years, thanks to Bob.

Voya con Dios, mi amigo!

W. Albert Brewer, M.D.

Twenty years ago Bob Carpenter came to the Arizona Medical Association as Executive Secretary. Since that time he has lived, breathed and, yes, even slept, working for "his doctors."

Twenty hours a day was no unusual event for Bob, day after day, Sundays included. No one could have been more devoted to his work.

Before ArMA and BOMEX were separated, Bob saw to it that every item on the application blanks was filled in correctly and accurately.

Such devotion to a job is seldom, if ever, found anywhere. We appreciate this more than mere words can tell. Bob, we hope you enjoy your well-earned retirement.

Carlos C. Craig, M.D.

Now that Bob Carpenter is about to retire, I'd like to add my accolades and a few reminiscences and perhaps in this way do honor to a man who was and is wholeheartedly dedicated to serving the interests of the doctors of Arizona.

I remember well the one expression that was typical of Bob and one that made the job of the elected representative of the Association so very much easier. It was, "We'll handle it," and he always did! There was no task too trying nor trifling to escape Bob's personal attention. Many times at night, on weekends and holidays when we needed Bob's help or advice we would find him at the office. As a matter of fact, it was standard procedure to dial the office number before dialing his home at odd hours, and almost always Bob would answer.

It was a pleasure to travel and room with Bob while on Association business. He took care of all of the details, was a most pleasant companion, always in good humor and never failed to have an incredible store of information at his finger tips when it was required.

After many years of association with Bob, I am persuaded that the Arizona Medical Association owes in large part to Bob its strength and usefulness to organized medicine.

I am proud to have worked with Bob Carpenter and to call him my friend. The experience has been rewarding to me personally and has shown that there still are men who are completely dedicated to giving the best that is in them to those to whom this loyalty has been pledged, in Bob's case to "my doctors."

Paul B. Jarrett, M.D.

With the retirement of Bob Carpenter, I am left with a feeling of vacancy, for he, of all people, has accomplished more for Arizona Medicine than anyone that comes to mind. His organizational ability and his diplomacy have weathered many stormy times, and the strength of our organization is, in great part, due to his efforts and understanding.

Personally, I feel a distinct loss because Bob and I started in Arizona Medicine about the same time — some twenty-plus years ago, and I grew through his help to take an active part in our organization. Without this help, I feel quite sure that what little I have had to offer would not have been forthcoming. Further, when I went on the Board of Medical Examiners, Bob again had the reins of organization, and through his efforts, I believe that great strides were made in the development of a far more effective Board.

One could go on at great length and express himself as to Bob and his value to organized medicine, but no one can ever adequately put feelings down on paper. I see Bob leave our organization with a sadness that comes when one loses an old and trusted friend.

I have missed working with Bob the past years but never will I fail to remember with great pleasure and gratitude all that he did personally for me.

W. R. Manning, M.D.

I feel fortunate that I have known Bob for a good long time. He wears well. To me he was an advisor, counsel and a helper out of the ordinary when I had the privilege of office in the Arizona Medical Association. It was up to him to indoctrinate and educate all of us who followed that path. Over the years he carried such responsibility with good success. His dedication has been absolute. His glowing personal pride in "his doctors" was evident on all occasions. He resented undue and unjustified criticism of the medical profession, probably more intensely than we did. His diplomacy was polished and persistently practiced in ways of subtle expertness. I am not convinced, however, that accolades, acknowledgments or memorials will do for Bob Carpenter all that we would hope it might. He should be pleased, however, to know that we recognize him as the architect of an ongoing healthy organization. He can also be assured that he has carved an indelible niche of acomplishment in the memory of each and every one of us. If good things can spring from good wishes, Bob Carpenter will hereafter be blessed in large measure. Aloha!

Dermont W. Melick, M.D.

"Most men will proclaim every one his own goodness: but a faithful man who can find?"

—Proverbs 20:6

It is with great pride of association and yet with deep humility in the recognition of my good fortune that I thank God for having worked with and known Bob Carpenter for over 20 years. During the early days of reorganization of the Arizona Board of Medical Examiners, the drafting of a new revised Medical Practice Act, the Incorporation of the Arizona Medical Association with its attendant revisions of the Constitution and By-Laws and innumerable long meetings, Bob's steadying influence and clarity of thought were valuable restraints upon an impetuous, hot-headed Abe Podolsky. For these, among many other blessed and valuable intelligent services, I am very grateful. I am also grateful for the opportunity to do honor to Bob in this issue of Arizona Medicine in according him the expression of appreciation he so richly deserves.

A lyrical eulogy of this man is not appropriate at this time — for he is still with us — not to be covered with a mantle of pale roses, but to remain as a warm, living memory of a man who dedicated many years of devoted and valuable service to "his doctors." He shall continue to remain valuable to the Arizona Medical Association for many years, even though in retirement, as a readily available source of information and wise advice. He has an encyclopedic store of knowledge of the Association's affairs and business, almost instantly recallable by a remarkable memory clearly, lucidly and intelligently presented.

A lesser man would only have performed a good job. His performance was superb! Despite his prodigious industry and diligence, he remained self-effacing, never complaining and quietly dynamic. When called upon, without preparation, for information, he always amazed me with his ability to deliver it promptly, with a warm spontaneity and with a presentation that was precise and succinct. Though his fatigue was visibly apparent, he never complained about long hours of service at an endless succession of major and minor committee meetings, so vital to the successful function of the Arizona Medical Association. One does not appreciate the many hours of unpaid-for overtime work that kept the lights burning late at night in the Association's offices, in the State Legislature and the long distances traveled in YOUR INTEREST AND MINE to meetings in all communities of the state and to national meetings.

He is a fine, warm, sincere gentleman at all times, even in those rare social occasions of relaxation over a drink with "his doctors." I can truthfully state that I have never heard Bob say a bad word about anybody. I have never felt that Bob, although he served the Association so well, was ever a "servant-employee" of the organization; instead he was a vital integral part, and probably "heart of the Association."

To Bob Carpenter I say, "I am honored and happy to have been, and I hope that I shall always continue to be your friend; for by your friendship and warm humanity, you have made me a better man." Bob has given me something to enrich my existence. He is another impetus to my work and a spur to my conscience and compassion. Having worked with this fine man has convinced me that the reason that we are here is to enhance the dignity of the human race.

He not only has my deep respect but my warm friendship. He deserves yours, too.

God Bless You, Bob and Mrs. Carpenter!

Abe I. Podolsky, M.D.

The realization that Bob Carpenter is retiring as Executive Secretary of the Arizona Medical Association is a bit of a shock. In the first place, I can hardly remember when he wasn't Executive Secretary, and of course, in the second place, many of us who are his long time friends must come face to face with the same decision.

The passing of time makes us think back into the past when the State Organization was much smaller, and when Bob had to do all the different aspects of the work of an Executive Secretary. I can remember far enough back when he had to smoke small cigars because the office in the Security Building wasn't big enough to permit him to handle the fine, big stogies he uses at this later time. Then, he did not only the work in the office, but made many trips to various parts of the State on Association business as well as smoothing feathers here and there and it was my privilege to be along on some of these efforts. Bob, you have helped the Association over many a hurdle and I hope you will live a long time in the understanding of our appreciation. I am sure the Association, in this fine new building, will always have a place for you to contribute your sage and helpful advice. I know from personal experience that it will be needed.

Oscar W. Thoeny, M.D.

Bob Carpenter and I started working for the Central Office of the Arizona Medical Association the same day in October, 1949. My father had had a light stroke, and I carried his resignation as Treasurer of the Association to the Council at its meeting at that time. I was appointed Treasurer to fill out the rest of the year term for him, and at that meeting Bob Carpenter was hired by the Association.

Of course, at that meeting, which was held at the Westward Ho, Bob met all the members of the Council, and you know how it is when one meets a number of people — you don't get all the names — you don't fix all the faces, etc. Some time later, probably a couple of months, I had occasion to be in Phoenix and went to the office of the Association. The secretary there, a hold-over from the days of Kitty Ives Coleman, as "Secretary to the secretary" knew me, but Bob was out of the office at the moment. She asked me to have a seat in Bob's office. When Bob came in I greeted him, he greeted me, and we started off talking about the affairs of the Association. After a while, since I appeared to have some knowledge of these affairs, Mr. Carpenter said to me "Just who do you represent?" and I realized then that not having reintroduced himself he hadn't placed me, but I said to him, "Well, I've been signing your pay checks for the last several months. Does that let you know?" and of course, Bob got red in the face and was a little bit flustered. Actually this was one of the few times I think in the years that he has been with the Association that I ever saw Bob flustered.

Bob Carpenter has given nearly 20 years of his life to the service of "his doctors" and we have been problems to him I know, but he never let up in his loyalty to the doctors, and he has been a loyal employee of the Association all this time. It has been his life, and he has labored long and hard to ease the work of Association officers.

The arrangements that have been made for his retirement are elaborate, but I know of no other employee who could deserve what the Board of Directors has planned for Bob Carpenter. Those of us who have worked with Bob during the years know that he is deserving of this sort of recognition from our Association.

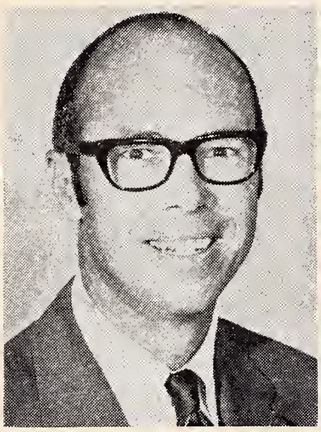
Organized medicine will lose a stalwart employee and fighter when Bob retires. I wish him God Speed and much happiness during his retirement.

Clarence E. Yount, Jr., M.D.

Topics Of Current Medical Interest

THE 'SIMBOL' RATING AND EVALUATION SYSTEM

A Measurement Tool for Injured Persons



RAYMOND E. WILLIAMS M.D.

JAMES L. SCHAMADAN M.D.

From the College of Engineering Sciences, Arizona State University and The Good Samaritan Hospial.
Reprint requests to Medical Director, Respiratory Therapy, The Good Samaritan Hospital, Phoenix, Arizona 85002 (Dr. Williams).

Synopsis - Abstract

The development of an Air Medical Evacuation System (AMES) in the state of Arizona revealed the need for uniform evaluation of accident victims. A rating system called SIMBOL was devised to meet this need. The SIMBOL, as presented in this paper, represents the rating system which has evolved from the operational marriage of concept and experience within the AMES program.

SIMBOL RATING SYSTEM

The purpose of the SIMBOL system is to provide a simple, yet meaningful guide to the evaluation of an injured person. The system is designed for use by anyone (first-aid trainees, medical technicians, nursing personnel, dentists, etc.) after one training-demonstration session.

The SIMBOL Rating. – The SIMBOL rating system uses a numerical scoring procedure for describing the present condition of an injured person, plus his potential for recovery. It reflects the "immediateness" of need for further medical treatment by underscoring not only present clinical condition, but also the probable rate of change of that condition. The scoring system is described as follows:

a. SIMBOL consists of two numbers, separated by a period, e.g., 8.6; 8.9; 3.4, etc. The first number(s) to the left of the decimal point is the "status" score. It indicates the present clinical condition of the patient thru a range from 0 to 10. Zero indicates a completely lifeless or moribund condition and a higher number (up to a maximum of 10) indicates an increasingly improved clinical status.

b. The number to the right of the decimal point is the "predictor" score. It estimates the potential for recovery. It considers factors that influence *rate of change* of a given clinical status. The higher the number, the more favorable is the prognosis. A low number indicates a rate of change consistent with a poorer prognosis.

c. The format of both the tables used for determining the SIMBOL rating are designed to augment and/or merge with the formats

TABLE I

PATIENT STATUS TABLE

SIGNS	VALUES		
	2	1	0
Pupils	small and responsive to light	unequal or sluggish	dilated, fixed
Pulse	between 60-100	less than 60 more than 100	absent
Respirations	between 10-20	less than 10 more than 20	absent
Blood Pressure (Palp Systolic)	more than 100	between 60-100	less than 60
OR			
Skin	dry and normal color	ashen, blue lips, moist	waxy, colorless or mottled
Level of Consciousness	awake, coherent	difficult to awake, sleepy	totally unresponsive

* Use Skin Color only when Blood Pressure has not been evaluated.

of familiar emergency care, first aid, or resuscitational programs already in existence. For example, the Patient Status Table (Table I) begins with an assessment of the pupils, pulse, respiration — the classic PPR of cardiopulmonary resuscitation training. In addition, the format of SIMBOL resembles the APGAR scale used for evaluating newborns.

USING THE SIMBOL SYSTEM

The "Status" and "Predictor" tables are printed on opposite sides of a wallet-sized card. These cards are carried by all AMES personnel and are posted in all the hospitals, ambulances, and aircraft in the AMES program. The cards are also distributed to all interested parties within the state.

Status Score. — The value of the left hand number (the status score) is determined from the Patient Status Table, as shown in Table I. The signs (pulse, blood pressure, skin color, etc.) are evaluated in the order listed and the values are added to obtain the status score. If a blood pressure cuff is not available, evaluate the patient using skin color rather than blood pressure.

Predictor Score. — The predictor number (number to the right of the decimal point) is obtained as follows:

a. STATUS Score (as determined
from Status Table) ....
Subtract 1 point each for:
b. WEIGHT: Markedly overweight ....
c. AGE: Less than 2 or over 70
years of age ....
d. TRAUMA:
Subtract 1 point for each of the following:
(1) over 50% of body burned
(2) open chest or abdominal wounds
(3) unconscious
(4) inability to move fingers and/or
toes in a conscious patient
PREDICTOR VALUE =
Sum of 1 + 2 + 3 + 4 above .....

The predictor value is sometimes called the SWT value, so named for its component parts — Status, Weight, Age, Trauma.

Exampels. Following are two examples in the use of the SIMBOL rating system:

Patient A. A 30 year-old housewife, thin, pale, and breathing very slowly (6 to 8 times per minute), is found in the rear seat of a car involved in an accident. Blood pressure is 70/40, pupils small, equal, and responsive to light, pulse is 130 per minute. She is rational and answers simple questions. There is no evidence of a chest wound and the lady states that she has felt the baby kick several times in the past moments. She can move her fingers and toes easily. SIMBOL 7.7

Patient B. (No blood pressure cuff available) A fat, 75 year-old school teacher was hit by a car. When evaluated, he was very groggy and incoherent, but he could move his fingers and toes. He was breathing heavily at 15-18 times per minute and his pulse was thready at 116; his color was sallow with blue lips, but his pupils were equal and reacted readily to light. No evidence of open chest or abdominal wounds. SIMBOL 6.4

The objectives of the SIMBOL system when originally used within Arizona's AMES program were two-fold. First, as an aid to insure uniform, thorough examination of every patient. In the process of obtaining the SIMBOL values, the para-medic performs an examination which assesses the status of all the patient's major systems (cardiovascular, respiratory, neurological, etc.), calls attention to major or life threatening injuries (burns, sucking chest wounds, paralysis, etc.), and then the evaluation is made to indicate the patient's expected recovery rate or potential. This last task closes the "learning-by-association" loop. Secondly, the SIMBOL is used as a measurement tool for making decisions or evaluations regarding medical services, logistics, mass casualties, triage, etc.

We believe that use of the SIMBOL system by the AMES para-medics has fulfilled the first objective mentioned above, i.e., to insure a thorough, uniform assessment of the patient's condition and expected recovery potential.

A great deal more experience is needed, in terms of numbers of patients, to be able to judge the degree of effectiveness achieved in meeting the second objective. If the SIMBOL system evolves as a useful measurement tool, it offers unlimited potential in the emergency care field.

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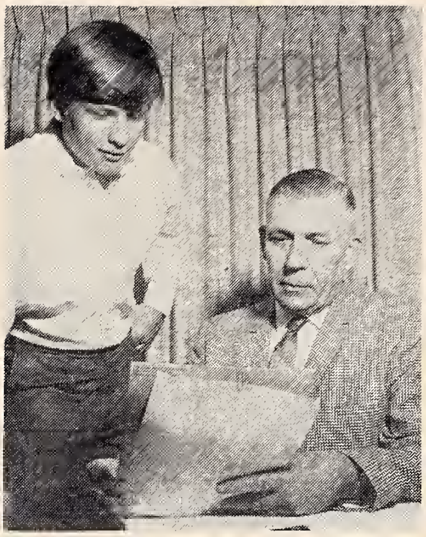
*This study was supported in part by the United States Department of Transportation, National Highway Safety Bureau Contract #FH-11-7090.



Norman Hovda, left, discusses DOPE STOP program with Frank Williams, Health Consultant, State Department of Public Instruction.

DOPE STOP

Gladys E. Conroy
Associate Director
Drug Abuse Education
Maricopa Mental Health Association

"Doing our own thing" is the sound which riccochets off the eardrums of the "establishment" to the far corners of households, classrooms and gathering places of youngsters today. Construing it from the positive approach, DOPE STOP, in its third phase called "Teen Involvement" has placed the responsibility in the hands of youth.

Junior and senior high school students in Maricopa County, as Teen Counselors, are accepting this responsibility of explaining to grade school students the dangers of drugs. Under the direction of Norman Hovda, Teen Coordinator for DOPE STOP, these high school students are learning about the consequences of drug abuse and, themselves, carrying the information to all 5th, 6th, 7th and 8th graders in the county. As the use of drugs creeps down into the lower elementary grades, physicians are reporting cases of youngsters experimenting as low as the third grade. Turned on by their older brothers and sisters, upper classmen and friends, children are reacting to the "kicks," lacking the maturity of reason and consequence.

Speaking out about the abuse of drugs on a student-to-student basis, the Teen Counselors emphasize that smoking "pot" and experimenting with dangerous drugs is no longer the "in" thing to do; and returning on a once a month visit to the same elementary classrooms, the students relate the latest facts on drug abuse. It is more or less the big brother (or sister) concept whereby the student stays with this class throughout the entire year — and on to graduation.

The Teen Counselors have been carefully selected by each high school administration, and their approach is to urge the students to make their decisions now regarding drugs, and not wait until they are approached and faced with the temptation. If questions arise concerning drugs on the part of the elementary school youngsters, the high school Teen Counselors will provide answers when they know them. If they do not know the answers, it is their responsibility to get the facts and bring them back to the class the next visit. Teen Counselors also give members of that class their home phone number and are available on a call basis between monthly classroom visits. Between visits to the grade schools the Teen Counselors have additional feedback and educational sessions with Norm Hovda. The high school Faculty Advisor also supervises the activities at the high school.

DOPE STOP Teen Coordinator, Hovda, speaks from three and one-half years experience as a drug user having formerly experimented with everything from marijuana to heroin and he can tell it as it is. "Communication of the real facts on drugs, hopefully, can show the students why playing with drugs is so dangerous and a waste of time." Curiosity is a strong factor in turning on to drugs, according to Norm, "but kids are curious about sex and booze, too. They just want to know what's happening. There might be some who will try it anyway, but if we can decrease percentages gradually, we will be showing progress."

Over 1,000 students are involved in the program. Training sessions for the Teen Counselors have already been held at almost half of the high schools in the County, and there is much eagerness among those who are participating as they are quick to recognize that it is their opportunity to accept the challenge of meaningful involvement. The training sessions are simple, and the students review the basic facts on legal and medical aspects of drug abuse.

Norman's enthusiasm for the program is infectious with the students, and this is manifested by the turnout at the training sessions. One high school in the Valley called out for volunteers and 120 showed up for screening and training — 40 more than needed. Encouraged and stimulated by the interest on the part of the students, young faculty members at the school are organizing the overflow into a club which will expound on the dangers of drug abuse right within the high school. One coed in the group expressed her feeling on Teen Involvement after a psychologist displayed some skepticism regarding the students ability to relate with the youngsters — "I don't use drugs — I don't think I'm square. I have a younger brother and sisters who are always interested in what I do."

"The training sessions reveal some wonderful people with some real good things to say," says Norman, "and if they can reflect their feelings as to why they are not interested in drugs, some real progress can be made in this area."

Norman talked about a young volunteer who had worked in a Psychiatric Ward at a local hospital. Her practical experience with some young people who hadn't come down from their "trips" gives her true insight into the dangers of drugs, and her related experiences can have real meaning to the kids. A young blind boy has found his own way of expressing himself —a way of fulfilling his own needs as well — by becoming vocal concerning drug abuse. On the whole, the students belie any skepticism on the part of the adults by their enthusiasm — and empathy — for the youngsters who are curious, but lack the facts about the dangers of experimentation.

Norman has his own story to tell — one which qualifies his involvement to set the pace for the Teen Counselors. He used drugs for about three and one-half years while attending Arizona State University full time. After many "trips" on LSD the last one sent him to Maricopa County General Hospital completely confused, paranoid and "spaced out." Five days of trying to find himself was enough of a horrifying experience for him to drop the drug habit and use his knowledge of their bad effects to prevent others from starting. Curiosity started him on marijuana while he was a Freshman, when offered it by a "friend." One thing led to another, and the same friend made available to him many of the legitimate drugs such as the amphetamines, barbituraates and opiates. "Once I got going, I was eager to try different drugs, but my fear of needles prevented me from shooting them. I guess I was just lucky in this case, but I was tempted many times. I did use heroin and other opiates on several occasions, but really preferred the psychedelics." Eighteen days after leaving the hospital when his prescribed tranquilizers ran out, Norman had a recurrence (or flashback) of his LSD experience which drove him to a point of near suicide. His religious background as a child turned him to the Bible instead.

As part of the second phase of DOPE STOP, Norman Hovda appears on panels before school assemblies, in combined class programs, churches and service organizations giving the facts on drugs and relating his own personal history with them. Currently the DOPE STOP Educational Program is reaching between 2,000 and 5,000 weekly throughout Maricopa County. In telling his story, Norman says he was not physically addicted to a narcotic — but was very much psychologically (and psychosomatically) addicted to "pot" and the psychedelics. He feels it definitely set the stage for his desire to try other drugs.

DOPE STOP, (a project of the Maricopa Mental Health Association) is the educational function of the CODAC structure (Community-wide Organization on Drug Abuse Control) and is funded in part by the State of Arizona, the County Board of Supervisors and several cities in Maricopa County.

SEPTEMBER 9, 1969

SLOW BUT SURE

SEPTEMBER 23, 1969

KARL S. HARRIS, M.D.

Born: November 2, 1909 – Lineville, Iowa.

Died: July 17, 1969 – Phoenix, Arizona.

Karl received his B.S. and M.D. degrees from the University of Iowa in 1934. He did his surgical residency at the University of Iowa Hospitals from 1938 to 1944. He was a Captain in Medical Corps of the U.S. Army from 11-4-41 to 12-2-42.

He was in private practice in Phoenix since July, 1944. He was a member of the staff of all the major hospitals in the Phoenix area. He also was a member of the following Medical Societies: American Medical Association; Fellow of the American College of Surgeons; Diplomate of the American Board of Surgery; Member of the Phoenix Surgical Society (President in 1958); Member of the Phoenix Trap and Skeet Club (Treasurer at the time of his death).

He is survived by his wife, Marjorie N. Harris; two sons, Keith H. Harris, M.D., and Jack N. Harris; mother, Alma S. Harris.

Karl was a dedicated doctor and surgeon as well as a husband and father. He gave a great deal to the Medical Community during his professional life here in Phoenix. All of us who knew him, had the highest regard for his honesty and moral integrity. His influences and effect on the medical circles will be felt for a long time in the future. He was dedicated ot the care of his patients and his profession as a doctor, and was highly respected by them.

Dr. Harris was prominent in the founding of the Phoenix Surgical Society and was among the first three Presidents of this society. He was a great sportsman. He loved to hunt as was borne out by his many trips to the Kaibab Forest and also in the Valley during White Wing and Dove Hunting seasons. He was also an avid skeet shooting fan, for which he had all of the necessary equipment; such as the loading of his own shells, etc. He spent many happy hours at these hobbies with his devoted and wonderful wife, Marjorie.

In thinking about Karl, I am reminded of the last stanza of "Thanatopsis".

"So live that when thy summons come to join
the innumerable Caravan,
Which moves to that Mysterious realm where
each shall take,
His chamber in the silent halls of death,
Thou go not, like the quarry slave at night,
Scourged to his dungeon, but sustained and
soothed.
By an unfaltering trust, approach thy grove
Like one who wraps the drapery of his couch
about him,
And lies down to pleasant dreams."

Good Luck, Good Hunting, and Good Skeet Shooting, Karl.

Henry G. Williams, M.D.

ROGER WHITE, M.D.

Roger F. White, a former Phoenix pediatrician, died on July 28, 1969 in the V.A. Hospital in Maryland.

Doctor White was a graduate of Harvard University in 1950. He interned at Grace New Haven Hospital in Connecticut, and served a residency in pediatrics at the University of California in San Francisco from 1951 to 1953. Though he has been absent from Phoenix for two years, it is doubtful that anyone who knew Roger – even casually – will have anything less than a clear and abiding remembrance of him, both personally and professionally.

He was a strong and forceful individual, and an energetic and tireless physician. He was a brilliant man and an exceedingly well trained pediatrician, being especially well-grounded in pediatric hematology.

Numberless children and young people in this community owe their present well being to his good pediatric sense and conscientious administration of medical care. He made an especially outstanding contribution to the care of Indian children in our state, both as a consultant at the Phoenix Indian Hospital and in the neonatal care of Indian babies at Good Samaritan Hospital.

It is with profound regret and a sense of immense loss both to the medical profession and the young humanity he did and would have continued to serve so well, that we mark his passing.

Derrill Manley, M.D.

SAMUEL WICK, M.D.

Samuel Wick died suddenly of coronary occlusion on Sunday, August 3, 1969, while enjoying a few hours of Sunday rest and relaxation in the midst of good friends, after his usual busy week devoted to his patients in the office, in the hospitals and to various civic organizations.

Doctor Wick was born sixty-three years ago in Wisconsin, received his B.A. at the University of Wisconsin in 1926, his M.D. from Rush Medical College in 1930. He then had intensive postgraduate training in psychiatry in Chicago, at Northwestern University, and at Marquette Medical School in Wisconsin.

After serving with the Air Force during the war years, from 1942 to 1946, as a psychiatrist, he entered private practice in Las Vegas for a short period and then became chief of the intensive treatment service at the Veterans Administration Neuropsychiatric Hospital in Sawtelle, California in 1952.

In 1953 he accepted a position at the Arizona State Hospital and served as its superintendent from 1953 until 1964, longer than any superintendent since statehood and during a period when Arizona State Hospital underwent its greatest expansion, both in numbers of patients and in regard to professional services, activities, etc.

Under Doctor Wick's guidance, most of the modern treatment modalities were introduced at the Arizona State Hospital, and the institution lost, hopefully forever, its custodial and rather backward reputation.

Doctor Wick, a Diplomate of the American Board of Psychiatry and Neurology, a Fellow of the American Psychiatric Association, and a certified Mental Hospital Administrator, elevated the professional standards of the Arizona State Hospital to the highest level possible in such an institution. He constantly fought the battle of limited and often woefully inadequate appropriations and drastic limitations of staff which he manfully attempted to overcome, at times quite successfully.

One most remarkable accomplishment during his entire superintendancy was his personal acquaintance and examination of every single patient upon admission and again upon discharge. Considering the great numbers involved, usually 1,600 admissions per year and an almost equal number of discharges, this feat becomes the more astounding. I doubt that it has been equaled in any similar institution in the country before or since. In the necessarily limited time that Doctor Wick could spend with each patient, he gleaned a remarkablly complete analysis of the background and the present symptomatology, and was able to dictate a concise and pertinent case summary for the guidance of less experienced staff members, as well as most helpful recommendations to be followed after discharge — all this in addition to his constant toil as administrator of a complicated institution.

It was this kind of devotion and total commitment to his life's work that made Sam Wick the truly exemplary physician whom we loved and admired.

An eleven year period of relative tranquility, peace and orderly advancement at the Arizona State Hospital was unheard of before Doctor Wick's administration, but finally the political axe came down once more and forced Doctor Wick to resign in 1964.

This tremendous loss to the State of Arizona was lessened by Doctor Wick's decision to remain in Phoenix and to enter private practice at the age of 58, and to his own great surprise, with outstanding success. The devotion to his profession and to his many patients, which he had developed over these years in institutional practice, was equally appreciated in private practice. The physicians of Phoenix, who had known Doctor Wick mainly as an administrator, learned to rely upon him as a trusted clinician, and the patients respected and loved him as an honored friend, counselor and therapist. His mature judgment, his kind counsel, and his great skill and wisdom will be missed by his many patients and in our professional circles and organizations where he was active to the last day.

Our sympathy and wishes go out to his wife, Lylyan, his sons, Alan, a geneticist, Gerald, a physicist, and Barry, a social worker, and his daughter, Barbara, a postgraduate student at the University of Wisconsin.

Otto L. Bendheim, M.D.

SYMOSIUM ON OPPORTUNISTIC INFECTIONS

November 29 and 30, 1969
SAFARI HOTEL
Scottsdale, Arizona

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ARIZONA PEDIATRIC SOCIETY
in cooperation with
NATIONAL COMMUNICABLE DISEASE CENTER
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GUEST SPEAKERS

MARK A. BELSEY, M.D.
Associate Professor of Pediatrics and Epidemiology, Tulane University School of Medicine

VINCENT A. FULGINITI, M.D.
Professor of Pediatrics and Head, Department of Pediatrics, University of Arizona

MOSES GROSSMAN, M.D.
Chief of Pediatrics and Isolation Services, San Francisco General Hospital and Professor of Pediatrics, University of California School of Medicine

WILLIAM G. THURMAN, M. D.
Professor and Chairman, Department of Pediatrics, University of Virginia School of Medicine

FEE: $10.00

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This symposium is acceptable for five prescribed hours by the American Academy of General Practice.

CLINICAL CARDIOLOGY

December 8-13, 1969

Del Webb's TowneHouse, Phoenix

Presented by: The American College of Cardiology and The Institute for Cardiovascular Diseases, Good Samaritan Hospital, Phoenix

An intensive six-day program covering in depth selected fields in cardiovascular diseases. The program is oriented toward practical application of diagnostic techniques, basic understanding of pathophysiology of heart disease and medical and surgical management of the most common problems in cardiology. The participants will be encouraged to become involved with interpretation of records on informal workshop type of sessions planned for the evening. This course is intended for those who want an extensive and detailed discussion of the current aspects of cardiovascular diagnoses and therapy.

ADVANCE REGISTRATION IS REQUIRED.

For additional information and application contact: William D. Nelligan, Executive Director, American College of Cardiology, 9650 Rockville Pike, Bethesda, Md. 20014.

Arizona Chapter American College of Surgeons

Arizona Society of Anesthesiologists

Joint Meeting

January 23-24, 1970

Arizona Inn, Tucson

For additional program information contact:

Rockwell E. Jackson, M.D.
5th and Alvernon Streets
Tucson, Arizona

PROGRAM ANNOUNCEMENT

The American College of Physicians Arizona Regional Meeting

FRIDAY AND SATURDAY—DECEMBER 12-13, 1969
SKYLINE COUNTRY CLUB—TUCSON, ARIZONA

FRIDAY, DECEMBER 12, 1969

A.M.

8:00 Registration

8:55 Governor's Introductory Remarks
ARIE van RAVENSWAAY, M.D.

9:00 Evaluation of Disability in Patients with Chronic Bronchitis and Emphysema
CARL DIENER, M.D., LOUIS J. KETTEL, M.D. and BENJAMIN BURROWS, M.D.

9:10 Long Term Continuous Oxygen Therapy in Chronic Airway Obstruction.
BERNARD E. LEVINE, M.D. and HOWARD M. KRAVETZ, M.D.

9:20 PANEL: Management of Acute and Chronic Obstructive Pulmonary Disease.
THOMAS M. FOREMAN, M.D., Moderator
LOUIS J. KETTEL, M.D.
ARNOLD L. SERBIN, M.D.
ROBERT E. WESTFALL, M.D.

10:20 Lymph Circulation in Congestive Heart Failure; Effect of External Thoracic Duct Drainage.
MARLYS H. WITTE, M.D., A. E. DUMONT, M.D. and R. H. CLAUSS, M.D.

10:30 Peripheral Vascular Effect of Digitalis Glucosides.
ROBERT M. ANDERSON, M.D., JAMES E. O'HARE, M.D., JAMES M. FRITZ, M.D. and RUBEN ACOSTA, M.D.

10:40 PANEL: Myocardial Revascularization.
JEROME C. ROBINSON, M.D., Moderator
EARL J. BAKER, M.D.
LEE B. BROWN, M.D.
LAWRENCE E. GANTER, M.D.
HUGH B. HULL, M.D.
DARREL D. SMITH, M.D.

11:25 Assessment of Patients Undergoing Home Maintenance Dialysis.
D. J. POTTER, M.D., and G. M. NICKAS, M.D.

11:35 Renal Function in the First Year after Kidney Transplanation — A Paired Donor-Recipient Study.
DAVID A. OGDEN, M.D.

11:45 PANEL: Diagnosis and Management of Chronic Renal Failure.
DAVID BEN-ASHER, M.D., Moderator
CHRISTIAN MENDE, M.D., Diagnostic Criteria; Management Before Dialysis.
KENNETH E. JOHNSON, M.D., Dialysis
DAVID A. OGDEN, M.D., Transplantation; Long Term Complications; Bone Disease; Anemia; Neuropathy.

P.M.

12:30 Luncheon: Presentation of the American College of Physicians Scholarship to a Member of the Junior Class of the University of Arizona College of Medicine.

2:00 Invitational Lecture.

3:15 The Role of Parathyroidectomy in the Patient on Regular Dialysis.
G. M. NICKAS, M.D., D. J. POTTER, M.D. and J. J. BERENS, M.D.

3:25 Thyrocalcitonin Excess.
MEYER MARKOVITZ, M.D.

3:35 PANEL: A. Calcium Metabolism.
B. Diagnosis of Thyroid Disease.
ALAN L. GORDON, M.D., Moderator.
RAYMOND F. GRAAP, M.D.
LAURANCE B. NILSEN, M.D.
STANLEY H. SCHNEIDER, M.D.

7:00 Reception.

8:00 Informal Dinner.

SATURDAY, DECEMBER 13, 1969

A.M.

8:00 Registration

9:00 HEMATOLOGY SECTION:
WILLIAM F. DENNY, M.D., Moderator.

9:00 Management of Chronic Idiopathic Thrombocytopenic Purpura.
ROY S. WEINRACH, Ph.D., M.D.

9:10 Purpura Due to Disorders of Platelet Function (Lo! The Wondrous Platelet).
OSCAR A. THORUP, M.D.

9:20 Discussion.

9:25 Metastatic Reticulum Cell Sarcoma, Hypercalcemia and Diabetes Insipidus.
NICK MANSOUR, M.D.

9:35 Anemias Associated with Decreased Erythropoietin Stimulation.
WILLIAM K. DENNY, M.D.

9:45 Non-Hemoglobin Proteins in Anemia.
A. H. WOODS, M.D., and PAUL O'BAR, M.D.

9:55 Discussion:

10:00 Disseminated Intravascular Coagulation and Fibrinolysis.
PAUL H. DUFFEY, M.D.

10:10 Interrelationship of the Complement, Inflammatory, and Coagulation Systems.
JOHN T. BOYER, M.D.

10:20 Discussion:

10:40 Student Award-winning Paper.
MEMBER OF THE THIRD YEAR CLASS, COLLEGE OF MEDICINE, UNIVERSITY OF ARIZONA.

11:00 Clinical and Phonocardiographic Recognition of Prosthetic Aortic Valve Ball Variance.
ALLAN I. COHEN, M.D., LEE B. BROWN, M.D. and ALBERTO BENCHIMOL, M.D.

11:10 Clinical Significance of Left Anterior Hemi-Block in the Electrocardiogram and Vectorcardiogram.
ALBERTO BENCHIMOL, M.D., E. C. BARRETO, M.D. and ANTONIO PEDRAZA, M.D.

11:20 Panel: Management of Cardiac Arrhythmias.
HERSCHEL M. RICHTER, M.D., Moderator.
ALLAN I. COHEN, M.D.
SHERMAN M. MINKOFF, M.D.
IRA B. EHRLICH, M.D.
GORDON EWY, M.D.

P.M.

12:05 LUNCHEON
Presentation of Awards to the Authors of the Outstanding Papers Submitted by Arizona House Officers and Medical Students.
SPEAKER: JAMES W. HAVILAND, M.D., President-Elect, American College of Physicians.
"The College, Today and Tomorrow"

1:30 Recent Advances in the Treatment of Pseudomonas Infections.
PAUL R. O'BAR, M.D.

1:40 Nitrofurantoin Lung Disease: A Case Report with Review of the Literature.
GERALD ALTSCHULER, M.D.

1:50 PANEL: Diagnosis and Management of Central Nervous System Infections.
DAVID RIFKIND, M.D., Moderator.
VINCENT FULGINITI, M.D.
JAMES W. HAVILAND, M.D.
WILLIAM A. SIBLEY, M.D.

2:35 House Officer Award-winning Paper.

3:10 Diagnosis and Management of Chronic Pancreatitis.
DAVID C. H. SUN, M.D.

3:20 Investigations in the Pathophysiology of Steatorrhea after Ileectomy.
CHARLES L. KRONE, M.D.

3:30 PANEL: Malabsorption.
ROBERT L. SOMMERVILLE, M.D., Moderator.
ROBERT KRAVETZ, M.D., Classification and Pathogenisis.
CHARLES L. KRONE, M.D., Diagnosis.
J. G. McGREGOR, JR., M.D., Management.

SCIENTIFIC PAPERS

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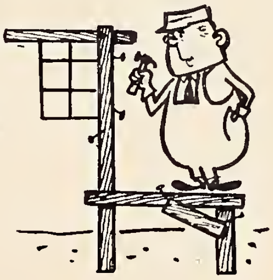
SCIENTIFIC EXHIBITS



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FOR THE 1970 ANNUAL MEETING
APRIL 21 - 25, 1970

EXHIBITS:

The Scientific Assembly Committee has arranged to expand and improve the facilities for scientific exhibits at the 1970 annual meeting. You are most cordially invited to develop an exhibit for the 1970 meeting. Send a brief description to:

Chairman — Scientific Assembly Committee
Arizona Medical Association
4601 N. Scottsdale Road
Scottsdale, Arizona 85251

Booth Spaces are 8′ wide and 6′ deep (two booths may be used if your exhibit is larger). All applications for exhibit space MUST BE MAILED BY DECEMBER 1, 1969. Set-up details will be mailed to you about one month before the meeting.

All Medical Directors are urged to encourage Interns, Residents and Fellows to participate.

(please indicate in your letter of application if more than one booth space will be required for your exhibit)

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PAPERS:

Again this year the Arizona Medical Association is soliciting papers from Arizona physicians for presentation at our Annual Meeting in April, 1970. We are particularily interested in having the Directors of Medical Education in our state's hospitals encourage the participation of their Interns, Residents and Fellows. The papers should be approximately one-half hour in length. A brief abstract should be mailed to:

Chairman — Scientific Assembly Committee
Arizona Medical Association
4601 N. Scottsdale Road
Scottsdale, Arizona 85251

The deadline for consideration is December 1, 1969.

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Should you have questions either about exhibits or papers please feel free to contact Bruce E. Robinson at ArMA headquarters. . .

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As is characteristic of sympathomimetic agents, it may occasionally cause *CNS effects* such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptics an increase in convulsive episodes has been reported.

Sympathomimetic *cardiovascular effects* reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others.

Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema.

Gastrointestinal effects such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported.

Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia.

A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

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The following 64 pages are reprinted from CALIFORNIA MEDICINE as an item in prospectus for a "Western Journal of Medicine," not yet in existence. It is proposed that articles of the kind shown here, with additional material from elsewhere in the western United States, be published in a supplement, to be called "The Western Journal of Medicine," which would be available at low cost for use in ARIZONA MEDICINE and in other selected journals from the Rocky Mountains westward, should they wish to use it. ARIZONA MEDICINE would of course maintain its present identity, treating "The Western Journal of Medicine" insert as additional material within its present cover.

Besides lowered cost, a great advantage of the combined circulation would be that the journal would attract writers who now place their scientific articles in publications that can offer wider readership.

The Management of Abdominal Injuries In the Presence of Head Injury

CHARLES B. WILSON, M.D., *San Francisco*

■ *When head and blunt abdominal injuries are combined, the head injury is often afforded too much attention and the abdominal injury too little, especially when the patient is unconscious. If mismanaged, the abdominal injury is often the more serious threat to life. Except for extradural hemorrhage, neurosurgical intervention, when indicated, can be delayed until the patient has been thoroughly evaluated for the presence of extra cranial injuries with higher therapeutic priority.*

Abdominal examination of the unconscious or uncooperative patient is difficult. Tenderness as a sign of abdominal injury cannot be elicited. Abdominal rigidity (in the absence of rigid extremities), a silent abdomen, shock, and extreme restlessness may indicate intra-abdominal changes. Abdominal paracentesis is a valuable diagnostic aid, and the finding of blood, bile-stained fluid, intestinal contents or air is an indication for immediate laparotomy. Once all injuries are known, priorities for treatment can be assigned. Often head and abdominal injuries can be treated concomitantly.

IN THE PRESENCE of combined head and abdominal injury some neurosurgeons as well as general surgeons tend to ignore the intra-abdominal trauma—the neurosurgeon because of his preoccupation with the head injury and the general surgeon because of his reluctance to carry out the usual and appropriate measures on an unconscious patient. The sins of both reflect a variable combination of misconceptions. Failure to recognize an intrinsically fatal injury is of less consequence than failure to recognize an injury that is fatal only because it is undetected or is not detected until it is at an irreversible stage.

The following remarks are directed to the general surgeon confronted by a patient with a head injury and known or suspected abdominal trauma.

From the Division of Neurological Surgery, University of California San Francisco Medical Center, San Francisco.

Submitted 28 May 1969.

Reprint requests to: Division of Neurological Surgery, University of California San Francisco Medical Center, San Francisco, Ca. 94122.

Recognition of abdominal injury concomitant with major head injury presents a problem since the usual criteria of intra-abdominal injury are masked.

Diagnosis: Head Injury

We can generally assume that the patient with visible evidence of head trauma probably has some degree of injury to the intracranial contents. If there is any historical, external, or x-ray evidence of trauma to the head, a patient must be managed as having a potentially serious head injury. This policy can do no harm, but to assume that a head injury is inconsequential simply because the patient was unconscious only briefly or not at all may be a serious error in judgment.

Unconsciousness is not tantamount to head injury; one cannot be equated with the other. Full consciousness depends upon simultaneous function of the cerebral cortex and the brain-stem reticular activating system. Loss of function in either system, whether due to hypoxia or mechanical injury, will lead to loss of consciousness. For example, the unresponsive patient with a scalp laceration may be unconscious because of asphyxia from airway obstruction or because of cerebral circulatory failure secondary to systemic hypovolemia.

A brief and systematic neurological examination may confirm suspicion of a head injury but abnormal neurological findings do not provide conclusive evidence of intracranial injuries. For example, major disturbances of motor function may follow injury only to the spinal cord or to more peripheral portions of the nervous system such as the brachial plexus.

Lumbar puncture can be omitted from this discussion, as it has no place in the diagnosis and treatment of acute head injury.

In the patient with known or suspected head injury, plain skull films should be taken but only after any necessary emergency treatment has been given. The value of radiographic examination is limited, but certain findings may be of great importance. Properly positioned films permit recognition of pineal shift, fracture into air-containing paranasal sinuses, fractures across the middle meningeal groove or a major venous sinus, the presence and extent of depressed fractures, and compound fractures not detected by physical examination. In addition, every unconscious patient should have anteroposterior and lateral x-ray studies of the cervical spine. Otherwise, cervical fractures may go undetected that may cause damage or add to injury already done to the spinal cord.

Diagnosis: The Abdominal Injury

In 1965, in collaboration with general surgical colleagues, I reported a study of 363 patients with blunt abdominal injury, one-fourth of whom also had head injuries.[1] Eleven patients died of unsuspected abdominal injuries; six of the 11 had a concomitant head injury. This experience indicated preoccupation with the head injury, misinterpretation of clinical signs, and insufficient attention to the abdomen. The mortality rate in patients with blunt abdominal trauma was four times greater when associated head injury was present, due in part to the confusion that head injury superimposes on the usual signs indicative of serious intra-abdominal trauma. From this experience emerged certain clinical precepts which bear repetition.

Tenderness cannot be elicited on abdominal examination of a comatose patient, and there may be equal difficulty in evaluating the patient with post-concussion confusion and somnolence. Deprived of the diagnostic information afforded by abdominal examination in a cooperative subject, the surgeon must rely on other evidence of intra-abdominal injury.

Abdominal rigidity cannot be ascribed to head injury unless rigidity is also present in the extremities.[2] If the extremities are flaccid or have normal muscle tone, a rigid abdomen connotes intra-abdominal injury. A head injury, no matter how serious, can cause neither abdominal rigidity alone, nor ileus. A silent abdomen following combined head and abdominal injury indicates either intra-abdominal injury or injury to the spine. Spinal cord transection causes prolonged paralytic ileus, and thoracic and lumbar vertebral fractures may produce ileus in the absence of injury to the spinal cord. Even in this situation the likelihood of associated intra-abdominal injury cannot be dismissed.

Misconceptions are slow to die and none has been more tenacious than the imaginary entity of central shock. Except as a terminal event, a head injury does not produce shock, and the finding of shock almost certainly indicates major injury elsewhere in the body.[3,4,7] To quote Meacham, "allowing oligemic shock to remain undisturbed and untreated while waiting for the nervous system to 'readjust' itself, perhaps feebly aided by the solicitous administration of vasoconstrictor drugs, is dangerous, and an error compounded by a reluctance to administer appropriate intravenous fluids to the brain injured patient."[5]

Not often is extreme restlessness seen following brain injury.[6,7] The patient with recent head injury is characteristically quiet and, in the absence of extracranial complications, prefers to sleep and be let alone. The appearance of restlessness demands immediate evaluation. It is most often caused by cerebral anoxia secondary to hypoxemia or hypovolemia, and second in frequency as a cause is pain due to over-distension of the bladder, unrecognized fractures, or extensive soft-tissue injuries. An uncommon but important cause of restlessness is the severe unilateral headache produced by extradural hematomas.

An earlier study indicated the safety and high diagnostic accuracy of abdominal paracentesis.[1] The finding of blood, bile-stained fluid, air or intestinal contents were an absolute indication for laparotomy. The type of needle used and whether peritoneal irrigation was done were much less important than the proper interpretation of a "negative" tap: the study referred to emphasized the limitations of a single negative tap, the value of repeated taps when indicated by clinical suspicion, and finally the mandatory requirement for laparotomy in spite of negative taps when clinical judgment called for laparotomy. In this last situation, a large retroperitoneal hematoma secondary to renal or skeletal injury often was found at operation. These facts strongly support a policy of routine peritoneal paracentesis in all patients with combined abdominal and major head injuries.

Management of Combined Injuries And Determination of Therapeutic Priorities

A thorough and systematic physical examination is a basic requirement for the management of a patient with serious head injury, and even in an unconscious patient the general examination should precede the neurological examination.[8] Vital signs will approximate normal values in cases of uncomplicated head injuries. Although a rapid rise in intracranial pressure produces bradycardia, a rising systolic blood pressure and slowing respiratory rate, in that order, a deviation of vital signs from the normal range is due much more often to extracerebral causes. Vital signs will also be disturbed in a patient with primary or secondary brain-stem injury with its associated decerebrate rigidity, tachycardia, hyperventilation and hyperthermia. With these exceptions a deviation of vital signs from normal values implicates extracerebral factors.

Management of major head injuries involves the care of unconscious patients. In an effort to avoid the aspiration of vomitus, a nasogastric tube is inserted soon after the patient is admitted. The flat, supine position is best for examination but should not be long continued because of the risk of aspiration. The patient should be maintained in a semilateral or semiprone position, with position changes from side to side at hourly intervals. In the absence of pulmonary complications and shock, the head is best kept elevated 20° to 30° to encourage venous return from the head. In this regard, the Trendelenburg position does not improve cerebral blood flow in a hypotensive patient, and venous congestion in the head-down position is clearly deleterious.

While over-hydration should be avoided, intravenous fluids need not be restricted because of head injury. In the absence of extraneous fluid loss, 2,000 ml of one-fourth or one-half normal saline solution per day should be administered intravenously. As a rule of thumb, intravenous fluid should provide a daily urinary output of about 1,000 ml. A patient with injury to the head retains salt and water for at least a few days after injury, and the slightly greater water retention produces mild hyponatremia.[9] In addition, because of an expanded extracellular volume, sodium excretion may be relatively large. The management of fluids in a patient with an uncomplicated head injury poses no problem. In replacing extra-renal fluid loss, the surgeon should take into account the usual metabolic response to head injury.

Neurosurgical indications will be mentioned only briefly.[7,8] The one true neurosurgical emergency is extradural hemorrhage. The typical patient has minor trauma to one temple, followed by a lucid interval of one to six hours, and then manifests signs of rapidly progressive compression of one cerebral hemisphere. This situation, and none other, is an indication for immediate neurosurgical intervention on suspicion. The emergency treatment of open head wounds is limited to the application of a sterile dressing with no attempt made to remove clotted blood or exposed brain. Definitive debridement can be delayed up to 24 to 48 hours without a significantly increased risk of infection, provided prophylactic antibiotic therapy is started promptly. Depressed skull fractures with an intact scalp are treated as closed-head injuries. Almost all depressed fractures should be corrected surgically but they rarely constitute an emergency. Deterioration of neurological function demands investigation by either carotid angiography[10] or bur hole inspection. The rate of deterioration determines the degree of emergency and the appropriate actions.

Among the intra-abdominal injuries, active intra-abdominal bleeding constitutes an immediate threat to life and surgical management is second in urgency only to extradural hemorrhage. Rupture of a hollow viscus is likewise an urgent situation, only slightly less compelling than active intra-abdominal bleeding.[7]

Unless the patient with intra-abdominal injury is in a terminal state from the associated head injury, laparotomy may be undertaken without delay. If there is a concomitant neurosurgical injury requiring operative management, judgment will dictate whether the two operations can proceed simultaneously or the cranial operation should be delayed. In general, unless the intracranial procedure would require several hours of operating time, the two can be done simultaneously once the patient's respiratory status and blood volume are returned to normal.

From what has been stated earlier, head injury does not constitute a contraindication to laparotomy, but rather dictates modification of the procedure customarily followed. An endotracheal tube should be in place during the laparotomy, and a short-acting anesthetic supplemented with muscle relaxants rather than deeper anesthesia should be used to obtain necessary operating conditions. Long-acting agents for pre-medication should be avoided and every effort should be made to begin and terminate the anesthesia quickly.

Conclusions

Meacham has stated that timely tracheostomy or blood transfusion has saved more lives in cases of head injury than all the other methods of supportive therapy combined, including exploratory bur holes for presumed hematoma. Emergency neurosurgical intervention is rarely a life-saving measure in patients with head injuries. By contrast, prompt surgical intervention for traumatic intra-abdominal bleeding saves many lives where both kinds of injury exist. The non-surgical management of head injuries follows fairly simple rules if one can separate misconception from fact. The general surgeon finds himself at a major disadvantage in evaluating the abdomen in the head-injured patient and in this regard abdominal paracentesis assumes a role of great importance. Because unrecognized intra-abdominal bleeding is a significant cause of death among patients with combined head and abdominal injuries, the general surgeon must adopt a more aggressive position in the handling of this common combination.

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The Management of Diabetic Coma

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Diabetic coma presents a medical emergency the outcome of which depends entirely upon prompt and knowledgeable medical attention. The mortality from diabetic coma at certain centers has exceeded 25 percent, while at other centers it is less than 2 percent.[1] We recently reported the treatment of 23 consecutive patients with no mortality.[2]

Evidence to indicate that mortality can be sharply reduced when an aggressive approach is adopted is provided by the classic report from the Massachusetts General Hospital in which mortality abruptly fell from 20 percent to 2 percent when a new routine of therapy was instituted.[3]

In recent years the pathophysiology of diabetic coma has been more precisely defined and has provided the foundation for a more rational management. The fundamental derangement is a relative or absolute deficiency of active insulin. The secondary derangements can be explained by the known effects of insulin.

The membrane of cells of the renal tubules and the cells of the central nervous system are permeable to glucose in the absence of insulin. Muscle call and fat cell membranes, however, are relatively impermeable until a sufficient concentration of circulating insulin acts upon them to allow glucose entry. In addition to its effect on membranes, insulin also brings about a modification in the way the liver manufactures glucose. With insulin deficiency, large quantities of glucose are produced by the liver and released into the circulation. Excessive glucose production and decreased cellular utilization combine to bring about increasing concentrations of glucose in the blood and extracellular fluid.

Such concentrations of glucose result in an osmotic gradient between the interior of the cells and the extracellular fluid which draws water and intracellular electrolytes into the extracellular fluid. The concentration of glucose in the glomerular filtrate is approximately the same as that of the blood. The osmotic diuresis which results carries large quantities of water and extracellular and intracellular electrolytes away in the urine. If hydration and renal function are maintained, the concentration of glucose in the blood rarely rises above 500 mg per 100 ml, since the renal loss of glucose serves to limit the degree of hyperglycemia. As renal function deteriorates, greater quantities of glucose accumulate in the blood.

The average adult presenting in diabetic coma has lost approximately six liters of water, 600 mEq of sodium, 400 mEq of chloride, 400 mEq of potassium, 400 mEq of bicarbonate, and 100 mM of phosphorous.[4]

Even in the absence of ketoacidosis, the dehydration and electrolyte imbalance brought about by extreme hyperglycemia can cause disturbed states of consciousness, progressing to profound coma. This condition has been termed hyperosmotic non-ketotic diabetic coma, and has been observed with increasing frequency since its description by Sament and Schwartz in 1957.[5] The blood glucose concentration in such cases generally ranges between 600 and 2,000 mg per 100 ml. Most patients with this form of diabetic coma are in the older age group and are found to have mild diabetes after the intense hyperglycemia has been successfully treated.

The reason such extreme hyperglycemia is not accompanied by ketosis is not clear, but recent evidence has been obtained to suggest that it may be the result of an ability to produce just enough insulin to suppress fat mobilization but not enough to promote adequate glucose utilization.[6]

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Insulin acts to suppress fat mobilization in two important ways. Fat in fat cells is present in the form of neutral fat which is a combination of one glycerol molecule with three long, fatty acid molecules. When this combination breaks, both the glycerol and fatty acids are released into the circulating blood. Once the break has occurred, the original glycerol molecule cannot recombine with the fatty acids, but a newly generated molecule of phosphated glycerol can take its place and fix the fatty acids within the cell before they escape into the blood.

Phosphated glycerol is one of the metabolic products of glucose which gains entrance to the cell through the action of insulin. When insulin is deficient, there is an insufficient production of phosphated glycerol to bind up liberated fatty acids.

Insulin acts in a second way to suppress fat mobilization through a direct inhibition of the reaction that produces the breaking off of fatty acids from glycerol. This inhibition may demand a smaller concentration of insulin than the indirect inhibition which results when insufficient quantities of phosphated glycerol are produced.

When free fatty acids are lost from the fat cells, they are carried to the liver, where they are degraded to the short chain acids beta-hydroxybutyric acid and acetoacetic acid. These two organic acids, along with the equilibrium product acetone, make up the "ketone bodies" of the plasma. The acids are highly dissociated in body fluids and readily produce excessive quantities of free hydrogen ions.

Hydrogen ions combine with bicarbonate ions to produce CO_2 and water. Both the increased concentration of CO_2 dissolved in the plasma and the increased content of hydrogen ion act on the respiratory center to produce the increased depth and rate of respiration characteristic of diabetic ketoacidosis (Kussmaul respiration).

The diagnosis of diabetic coma is suggested by the clinical state and supported if glucose or ketone is found in the urine. The diagnosis is confirmed, however, only when abnormal concentrations of glucose or ketone are found in the blood. Many comatose patients who are not in diabetic coma may have glucose or ketone in their urine.

Because of the importance of beginning treatment promptly, the diagnosis cannot be delayed while specimens are sent to the laboratory, nor can treatment be guided by determinations from the laboratory because there is no time to wait for them.

It is, therefore, important that the diagnosis be made and subsequent management guided by simple bedside laboratory tests in combination with the clinical findings. Fortunately such tests are available. The blood glucose concentration can be estimated with glucose oxidase strips and the plasma ketones can be estimated with nitroprusside tablets.

Several milliliters of blood should be drawn into a heparinized tube. The specimen is divided into two parts and one is briefly centrifuged. A drop of the uncentrifuged specimen is applied to a glucose oxidase test strip (Dextrostix®, Ames). If the concentration is greater than 250 mg per 100 ml, which is the highest concentration registered with Dextrostix, subsequent serial dilutions with saline solution should be made to estimate the magnitude of the blood glucose concentration. A strongly positive reaction with one part blood to two parts of saline solution provides strong supportive evidence for a diagnosis of diabetic coma, even if ketones are absent.

One drop of plasma from the centrifuged portion of the specimen is placed on a nitroprusside impregnated tablet (Acetest®, Ames). In diabetic ketoacidosis, the tablet will turn dark purple within two minutes. If such a reaction occurs, it can be assumed that the blood acetoacetic acid content is greater than 30 mg per 100 ml, which in our experience occurs only in diabetic ketoacidosis.

All normal persons have varying concentrations of acetoacetic acid in their plasma at all times, and in certain circumstances, such as simple starvation, the concentration may be greatly increased. Such levels, however, do not reach those found in diabetic ketoacidosis. The use of intact nitroprusside tablets provides a test which is desirably insensitive and will separate diabetic ketoacidosis from all other forms of ketoacidosis. Not to be used for this purpose are crushed nitroprusside tablets or nitroprusside powder or test paper, as these give a more sensitive test which may be misleading. We have seen nitroprusside tablets over which an oxidation crust has formed, so that they do not readily detect the presence of acetoacetic acid in the serum. If this is suspected, the flat surface of the tablet should be rubbed on a coarse paper towel before the serum is applied.

With the great mobilization of fat which occurs in diabetic ketoacidosis, the serum may at times be so lipemic that the color of the nitroprusside tablet cannot be properly observed. If this occurs, a drop of the lipemic plasma should be placed on the Acetest tablet and after two minutes should be scraped or blotted off so that the color can be observed. The test is still valid in these circumstances.

If a strongly positive test on the intact tablet is found, it is not necessary to make serial dilutions of the serum before treatment is started, but the plasma should be saved so that this may be done at a later time when comparison with subsequently drawn specimens will provide an index of the efficacy of treatment. A part of the original blood specimen or plasma should be sent to the laboratory for quantitative determination of glucose, urea and electrolytes.

As soon as the diagnosis of diabetic coma is established, an intravenous infusion with an 18-gauge needle should be started. The initial dose of unmodified (crystalline-zinc) insulin should be injected intravenously at that time.

In determining the dose of insulin to be administered, one should not be governed by considerations of how little insulin might be given to obtain desired effects but rather how much insulin may be administered without danger. Patients with ketoacidosis are very resistant to insulin. Statistically, the mortality rate for patients receiving smaller initial doses of insulin is significantly higher than for those receiving larger doses.[7] Although it was originally felt that patients with hyperosmotic non-ketotic diabetic coma might be successfully managed with smaller doses of insulin, additional experience has indicated that survival is increased when quantities of insulin similar to those used in ketoacidosis are employed.[8]

If the patient has cloudy sensorium, and the blood glucose is 250 mg per 100 ml or greater *and* the plasma or serum is strongly positive for acetone, we initiate therapy with 200 units of regular insulin intravenously. If the blood glucose is estimated to be over 750 mg per 100 ml by the glucose oxidase test, we use a similar dose of insulin even though the reaction for serum acetoacetic acid is not strongly positive, or is even absent.

We strongly recommend that all insulin be given intravenously, not only to obtain the most rapid effect from the dose administered but because there is less tendency for a prolonged insulin effect extending to a time when it might be undesirable. The action of subcutaneously administered insulin may persist for six hours or longer.

Only after the initial dose of insulin has been administered and the infusion of intravenous fluids initiated is the serial dilution of plasma necessary for a more accurate estimation of the acetoacetic acid concentration. Blood specimens are drawn at intervals of approximately one hour and subjected to such determinations. The second dose of insulin should be given only after the concentration of glucose and acetoacetic acid in the blood specimen obtained after one hour has been compared with that in the first specimen.

If the concentration of blood glucose (non-ketotic hyperosmotic coma) or serum acetoacetic acid (ketoacidotic coma) has not fallen, or if it is greater than it was initially, another large dose of insulin is injected intravenously. This second dose should be of the same order of magnitude as the first. If, on the other hand, the concentration of blood glucose or serum acetoacetic acid is found to be less than it was initially, a dose of insulin approximately half that of the first one should be given.

In the therapy of ketoacidosis, insulin dosage is based primarily on the concentration of plasma acetoacetic acid. Any time the concentration of acetoacetic acid is found to be less than that obtained an hour before, the dose of insulin injected is approximately half the one preceding. If, however, the concentration of acetoacetic acid is not significantly different from that in the preceding sample, the dose of insulin is either the same as or greater than the one before. If at any time the concentration of acetoacetic acid is found to be increasing, the dose of insulin should be doubled each hour until this trend is reversed. Occasional cases of insulin resistance will be encountered in which thousands of units of insulin are necessary to produce a decrease in the concentration of acetoacetic acid.

Frequently the blood glucose level will fall below 200 mg per 100 ml before acetoacetic acid has disappeared from the plasma. When this occurs, insulin should be continued and hypoglycemia prevented by the infusion of glucose-containing solutions.

In the therapy of non-ketotic hyperosmotic diabetic coma, whenever the blood glucose is estimated to be significantly less than that of an hour before, the dose of insulin should be approximately half of the preceding dose. If the blood glucose concentration is not less, however, the same dose should be repeated or a larger dose given. Generally, hourly doses in the range of 100 to 200 units are continued until blood glucose falls below 500 mg per 100 ml.

It must be borne in mind that although the patient in diabetic coma has lost large quantities of sodium, he has lost an even greater volume of water. Sodium replacement should therefore always be in the form of hypotonic solutions. This is even more important when treating non-ketotic hyperosmotic coma.

Replacement with 0.45 percent saline solution is recommended. An attempt to hydrate the patient with normal saline solution will not provide the free water that is needed.

Patients recover from ketoacidosis more quickly and become responsive to insulin sooner if alkali is administered early in the treatment program. Blood pH generally ranges from 6.8 to 7.2 and is usually below 7.0 if the patient evidences serious sensorial changes. Therefore, as an initial replacement solution, we recommend half normal saline solution with one vial of sodium bicarbonate (containing 44 mEq) added to each liter. Such a solution has the advantage of providing some free water, of furnishing relatively more sodium than chloride, of providing an alkaline solution and of not containing glucose, which would contribute to an already elevated glucose level and produce a further increase in the osmolality of the extracellular fluid.

The first liter on this solution should be administered within 15 to 20 minutes, and the next two liters should be given over the following 90 minutes. Additional fluid at a rate of 500 ml per hour during the next four hours is usually adequate.

When the patient with diabetic coma is admitted to the hospital, his total body potassium is decidedly depleted, and the serum level reflects dehydration and renal insufficiency with or without acidosis. It is, therefore, expected that soon after the initiation of treatment with insulin and hypotonic saline solution, the serum potassium will fall rapidly to subnormal concentrations. It is difficult to obtain accurate values of serum potassium quickly from the laboratory, and the electrocardiogram correlates poorly with the initial serum potassium level. We therefore routinely begin the administration of potassium soon after effective treatment has been initiated and urine flow established. We recommend the administration of potassium one to two hours after the beginning of treatment, to be continued at the rate of 20 to 30 mEq per hour for the next five or six hours. It is further recommended that, when it is available, potassium be given as the phosphate or acetate salt.[9]

Hypotension may occur either as a presenting sign or late in diabetic coma. The hypotension which is part of the presenting manifestations is often due to severe volume depletion and usually responds to intravenous fluid replacement. If the hemotocrit at first is low-normal, or is low in spite of a pronounced deficit in fluid volume, these patients often will require blood transfusions. In this circumstance one must consider acute hemorrhagic pancreatitis as the cause of the diabetic ketoacidosis and the blood loss anemia.

The later occurrence of hypotension may reflect diminished peripheral resistance secondary to inappropriate vasodilation and is often responsive to the administration of norepinephrine.[10]

When an aggressive approach to the treatment of diabetic coma is undertaken, the patient is usually in a satisfactory state of control within four to six hours, and often wants to eat and drink at this time. We advise prohibiting oral intake for at least 12 hours, because earlier feeding often causes nausea and vomiting.

After the blood sugar is below 250 mg per 100 ml and acetoacetic acid has been eliminated from the plasma, control can be continued by subcutaneous injection of small quantities of crystalline insulin. It is given every four hours and the dose is determined by urine testing. Generally, the patient can be returned to his usual routine of diabetic management the following day.

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Rubella

Technical Problems in the Performance of Hemagglutination-Inhibition (HI) Tests

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■ *The rubella hemagglutination inhibition* (HI) *test is the most sensitive serologic method available for diagnosis of infection and for determination of immunity status. At present, however, it is not a well-standardized procedure and several modifications are in use. Comparison of results obtained on the same specimens by different laboratories has shown wide variations. The sensitivity and reliability of the technique is decidedly influenced by each of the variables of the test system; these include erythrocytes, antigen, methods employed for removal of nonspecific inhibitors and natural agglutinins from test sera, the pH of the diluents and the temperature of incubation. The presence or absence of* HI *antibody cannot be determined reliably by screening a single low dilution of serum. Commercially available reagents and kits for rubella* HI *tests vary widely in their reliability. The test should be performed only by experienced persons who understand the principles of the technique and who are aware of the pitfalls and of the importance of using adequate controls in each run.*

THE HEMAGGLUTINATION-INHIBITION (HI) test[1,2] is the most widely used procedure for determination of rubella (German measles) antibodies. These tests are now commonly employed in clinical practice for the diagnosis of suspected cases of rubella, especially in pregnant women and their immediate contacts and for determining the immune status of pregnant women exposed to rubella.[3,4] The results of the test and their interpretation may be a determining factor, of considerable concern to the physician and patient. in judgments as to clinical management.

The impending release of live, attenuated rubella virus vaccines[5] will very likely create a sharply rising demand for rubella HI tests to identify susceptible adolescent and adult women of childbearing age who should be immunized. The risk that the live virus vaccine may result in injury to the fetus if given during pregnancy or shortly before conception, is unknown. Hence administration of the vaccine is absolutely contraindicated during pregnancy and a woman of childbearing age may be given the vaccine only if she understands that it is imperative for her to avoid becoming pregnant

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for the following two months.[5] The question of whether or not to administer vaccine to a patient of childbearing age is resolved if it can be established by a serologic test that she already possesses antibodies (approximately 75 to 80 percent have antibodies by age 20).

With the development of HI techniques for measuring rubella antibodies and the recent availability of commercial testing kits and reagents, a number of laboratories which have not had previous experience with HI methods are interested in undertaking rubella tests. At present, however, the HI test for rubella is not a standardized technique and several modifications are in use.[1,2,6,7,8] Comparison of results from different laboratories on the same specimens has shown wide variation. The Medical Laboratory Services Advisory Committee to the Public Health Service has recently warned: "This test is a complex procedure which must be performed by well trained, experienced individuals. In addition, a thorough knowledge of the immune response is essential for the proper interpretation of test results. Because of actions which may be taken on the basis of laboratory results, the need for accuracy is great, and certain problems associated with the HI test must be recognized."

The Viral and Rickettsial Disease Laboratory of the California State Department of Public Health and other virus laboratories are collaborating with the National Communicable Disease Center in Atlanta to assess certain variables in the test and arrive at a standard recommended procedure. The following outline of some of the technical factors and pitfalls in rubella HI test and reagents now in use will assist in understanding the types of difficulties a laboratory is likely to encounter and the wide variation in results on the same specimen which may be obtained by different laboratories.

Technical pitfalls in rubella hemagglutination-inhibition (HI) *tests*

A. Components of the rubella hemagglutination and hemagglutination-inhibition systems.

1. Hemagglutinating (HA) antigens

a. *Potency of antigen*

Usable rubella HA antigen preparations may vary in titer from 1:32 to 1:1024. Antigens of low titer may contain non-hemagglutinating viral particles which compete with hemagglutinating particles for antibody, and thus give lower antibody titers than those which are obtained in tests with high-titered antigens in which non-hemagglutinating particles are diluted out. Since low-titered HA antigens tend to give tests of low sensitivity, "false negative" results may be obtained. Antibody titers of a given serum may vary as much as 8-fold against different antigen preparation.

b. *Effect on antigen titers of other variables in the test system.*

The HA activity of rubella antigens is dependent upon the pH of the diluents, the temperature of incubation and the erythrocytes in the tests. Failure to use optimal pH, temperature and erythrocytes results in less sensitive tests—that is, reduced ability to detect antibody.

c. *Avidity*

Rubella HA antigens prepared by different procedures may vary in their avidity—that is, in their ability to combine with specific antibody. The reasons for these differences in avidity are not known, but may be related to the presence of non-hemagglutinating viral particles in the preparations.

d. *Treatment with chemicals*

To be acceptable and safe for use in diagnostic laboratories, the infectivity of rubella virus HA antigens must be destroyed by treatment with Tween-80 and ether. This may produce changes in the reactivity of the antigen as evidenced by erratic settling of agglutinated erythrocytes and even in spontaneous elution of the hemagglutinins from agglutinated erythrocytes.

2. Diluents used for various reagents

In some of the currently-used rubella HI test procedures the diluents are buffered to give the optimal pH for hemagglutination (pH 6.2) while with other procedures the diluents do not give an optimal pH for rubella hemagglutination. In the latter case the test is less sensitive for detection of antibody. The stability of the antigen may also be influenced by the diluent in which it is suspended. Some of the test procedures employ diluents containing a low concentration of bovine albumin, which facilitates settling of the test erythrocytes and aids in reading the results; others do not. Since the products from each manufacturer are for use in a specific procedure, intermixing reagents from different sources may alter the performance of the test.

3. Erythrocytes used in test

It is essential to use only those species of erythrocytes which are most sensitive to agglutination by rubella virus, viz., pigeon or one-day-old chicken erythrocytes. Failure to do so results in tests of decreased sensitivity. Also, as different lots of cells may vary in their sensitivity to agglutination, a reliable source of erythrocytes of consistent sensitivity is a requisite.

Erythrocytes should be stored no longer than two weeks before use in rubella HI tests. Older erythrocytes hemolyze, tend to agglutinate spontaneously and become less sensitive to rubella hemagglutinins. Some commercially available erythrocytes which have been treated with a preservative to increase their shelf-life have been found to give indistinct patterns of hemagglutination and inhibition, so that accurate reading of results is difficult for the experienced worker, and virtually impossible for the inexperienced.

4. Sera to be tested

a. *Natural agglutinins*

Human sera normally contain natural agglutinins for the test erythrocytes, and these must be absorbed from the sera before valid test results can be obtained. It is important to determine the proper amount of erythrocytes which effectively remove agglutinins and to absorb the sera at 4°C. Human sera appear to contain higher levels of natural agglutinins for pigeon erythrocytes than for chicken erythrocytes and with certain sera it is difficult to absorb out these agglutinins. Residual agglutinins will mask antibody reactions in lower serum dilutions, giving a "false negative."

b. *Nonspecific inhibitors of hemagglutination*

All sera contain fairly high levels of nonspecific inhibitors of rubella virus hemagglutinins. These must be removed from the sera before they are examined for specific antibodies. Failure to remove inhibitors results in "false positive" reactions. Some of the treatments, however, may remove specific antibody as well as non-specific inhibitors.

At this time kaolin treatment is most widely used for removal of rubella HA inhibitors. The koalin must be acid-washed, and it should be recognized that different batches of koalin may vary in their ability to remove inhibitor. The greatest drawback to the use of koalin is that it may remove specific antibody, particularly IgM antibody. The use of koalin suspended in a buffer at pH 9.0 minimizes absorption of antibody, but not all of the test systems employ koalin at this pH.

The non-specific inhibitors of rubella HA are in the beta-lipoprotein fraction of serum, and this can be specifically precipitated with heparin and $MnCl_2$ without removing specific antibody from the serum. At this time procedures for heparin-$MnCl_2$ treatment are not well standardized. Using too little of the reagents results in incomplete removal of inhibitor, and using too high a concentration of the reagents causes the test serum to agglutinate the test erythrocytes. If sera to be treated with heparin-$MnCl_2$ are diluted in a phosphate buffer, a precipitate is produced which removes specific antibody from the serum.

B. Conditions of incubation of the tests

Rubella hemagglutination occurs optimally at 40°C, although the reaction also takes place at higher temperatures. Some of the test procedures currently in use employ incubation at room temperature; this results in a less sensitive test.

C. Test controls

The dilution of antigen employed in the test must be "back-titrated" to determine that the proper number of antigen units was used. Using too little antigen results in false positive results, while too much antigen gives false negative results. Most test systems employ four units of antigen.

Every test run must include a known negative serum and a positive serum of known titer. The negative control serum should show no inhibition of hemagglutination at a dilution of 1:8 or 1:10, while the titer of the positive serum should vary no more than two-fold from the known median titer. If such results are not obtained in the controls the test is considered invalid.

At least four of the lower dilutions of each test serum should be examined for possible ability to agglutinate the test erythrocytes (incomplete removal of natural agglutinins). If the serum dilutions alone produce agglutination specific rubella antibody, if present, is masked.

Every run must include a number of "erythrocyte controls" consisting of the test dose of erythrocytes and the diluent used for the serum and virus. This indicates whether the erythrocytes settle properly under the test conditions. Erythrocytes frequently will not settle in improperly cleaned plates or tubes, and this can be mistaken for agglutination.

D. Screening

The presence or absence of rubella antibody cannot be determined reliably by testing only a single, low dilution of serum. Nonspecific agglutination caused by natural agglutinins in serum or improperly cleaned test vessels can lead to incorrect results, which can be recognized only if a range of serum dilutions, dilutions beyond the highest expected serum titer, are tested. Also, determining antibody endpoints can aid in determining the relative sensitivity or insensitivity of each run.

E. Observations on rubella HI test reagents from various commercial sources.

The following observations on commercially available reagents, taken from the experience of this laboratory or reported to us by other laboratories, illustrate the variations or problems which may be encountered. However, manufacturers are continuously striving to improve their products, and difficulties encountered with one lot of a reagent may not apply to other lots from the same manufacturer.

Manufacturer A. Antigens, reference sera and erythrocytes from one-day-old chickens are available. Experience in this laboratory with these reagents has been limited to a single lot of HA antigen referred for testing by a local public health laboratory. The antigen gave a titer of only 1:4, while the indicated titer on the label was 1:32. This antigen was thus not satisfactory for use in rubella HI testing.

Manufacturer B. Kits containing all of the reagents necessary for rubella HI testing are available. The test system does not utilize what is generally regarded as the optimal pH for rubella hemagglutination, and the koalin is not suspended in buffer at pH 9.0 to minimize antibody absorption. Difficulties have been encountered with low titers of certain lots of antigen, both in this laboratory and in a reference virus laboratory. The patterns of hemagglutination and inhibition produced by the preserved erythrocytes furnished with the kit are difficult to read or interpret.

Manufacturer C. Kits for rubella HI testing are available containing all of the reagents with the exception of erythrocytes, which can be obtained separately. The test system employs the optimal pH for rubella hemagglutination and koalin is suspended in buffer at pH 9.0. In the experience of this laboratory, and also the reference laboratory, the reagents have been found to be satisfactory, and the antigens have been of high titer.

Manufacturer D. Rubella HI testing kits are available. This laboratory has had no experience with the reagents; however, a reference laboratory found the titers of the antigens to be too low for satisfactory performance.

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CASE REPORTS

Benign Micturition Syncope

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THE SUDDEN DEVELOPMENT of unconsciousness in a previously healthy, young or middle-aged patient is always an alarming incident. Unless the reason is immediately apparent a physician must consider and rule out such serious entities as brain tumor, stroke, myocardial infarction and epilepsy. In recent years attention has been drawn to a clinical syndrome in which syncopal attacks associated with urination occur *de novo* in apparently healthy young and middle-aged men. This has been designated "micturition syncope."[1] Although only a dozen cases so diagnosed have been reported, it is felt desirable to bring the attention of physicians to this syndrome. For recognition of the phenomenon and knowing it is invariably benign will permit the omission of costly and time-consuming diagnostic studies and spare the patient much anxiety.

Report of a Case

The patient, a 45-year-old white male schoolteacher, considered himself in excellent health until he had a syncopal attack. The patient said he arose at his usual hour of 6:00 a.m., feeling completely normal. While performing the first micturition of the day in a normal fashion he suddenly became nauseated, felt faint and soon lost consciousness. His wife said she heard him fall to the floor, and then rough, stertorous breathing. She found him propped in a corner of the bathroom completely unconscious, his hands and jaws moving convulsively. After an estimated four or five minutes he became conscious and recovered normal function. On medical examination approximately two hours later, he said he had no residual effect except weakness and considerable apprehension. There was no history of urgency or pain or difficulty in starting the urinary stream. Specifically questioned, the patient denied straining to initiate the stream and he had no previous history compatible with prostatism, nor of bleeding, polyuria, polyphagia, nausea, vomiting or dark or tarry stools. He had had no chest pain at the time or previously and no respiratory distress. He could not recall coughing at the time of the syncopal episode or for several weeks preceding. He had had no similar episode in the past, had never previously fainted or lost consciousness and had no history of head injury. He neither smoked nor drank and was taking no medication.

On physical examination the patient appeared quite apprehensive and the skin was somewhat ashen. The pulse rate was 60 and blood pressure was 160/90 mm of mercury. No abnormality was noted on neurologic examination. Because of the somewhat unusual circumstances surrounding this episode of fainting the patient was admitted to hospital for observation. Results of physical examination there remained entirely within normal limits and the initial elevation of the blood pressure did not recur. The blood pressure in the hospital averaged 130/80 mm. The stools were always brown and several specimens were negative for occult blood by the usual tests. Several electrocardiograms were normal. An x-ray film of the skull showed no abnormality. The hemoglobin was 14.1 grams per 100 ml of blood and the hematocrit 44 percent. Leukocytes numbered 7,250 per cu mm with a normal cell differential. The fasting blood sugar on the day after admission was 110 mg per 100 ml. Specific gravity of the urine was 1.010 and it was negative for albumin, sugar and acetone. No unusual features were found in the urinary sediment.

As the blood pressure quickly returned to normal in this patient, there appeared no reason to look for pheochromocytoma.

Submitted 5 May 1969.

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No further episodes nor any other abnormal symptoms occurred in six years of follow-up of this patient and he remains clinically well.

Comment

Strangely, the first reference to syncope specifically associated with micturition did not occur until 1958. In the report of syncopal episodes of varied causation in 82 presumably healthy young adults, urination is listed as the "clinical incident associated with syncope" in four.[2] In one of these, however, "fatigue—lack of food—alcoholic ingestion" are also noted, without further comment. In another the patient was in the hospital because myocardial infarction was suspected, and although that suspicion was not substantiated, it at least suggests the added factors of anxiety or functional disease. Nausea was also a symptom in that case.

Since then ten additional cases of what has been called micturition syncope have been described.[1,3,4]

In only one of the 12 cases was urinary tract disease demonstrated.[1]

The following factors were common to the remaining 11 cases, as well as the present one: All the patients were men between 23 and 60 years of age (most between 30 and 46). The episodes occurred at night, almost always soon after arousal from sleep, the act of urination was begun without straining, was painless, free and without symptoms; and the syncopal episode occurred after some urine was passed or after passage was complete. Recurrence is unusual.

The cause of micturition syncope is unknown. Proudfit and Forteza[3] have expressed the opinion that Valsalva's maneuver with decreased venous return is responsible. They imply that the maneuver is a normal component of the act of micturition in males. In the normal male without obstruction, straining does not appear necessary to initiate urination, and the act of cessation of urination is aided by voluntary contraction of the bulbocavernosis and ischiocavernosis muscles. In the seven cases described by Proudfit and Forteza none of the patients is reported as making mention of Valsalva's maneuver.

Etiologically, micturition syncope would appear to be the summation of several physiologic phenomena. It is known that the sudden, rapid shift from the horizontal to the upright position may result in syncope in some persons.[5] The quiet, erect posture in the male during micturition before he has begun any muscular activity may also contribute to orthostatic hypotension, a situation akin to fainting in soldiers kept at rigid attention. That these postural factors are operative would seem supported by the fact that this syndrome has never been reported in women.

If the Valsalva maneuver were a frequent cause, should not one expect both frequent recurrence and at least some instances during the day?

Summary

A case of micturition syncope is described and the 12 cases previously reported are reviewed.

It appears likely that the cause is not the performance of a Valsalva maneuver, as has been suggested, but rather a summation of failure of orthostatic blood pressure mechanisms.

The condition is benign and unlikely to recur.

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Porphyria Cutanea Tarda Remission by Venesection

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PORPHYRIA CUTANEA TARDA describes a biochemical abnormality characterized, chemically, by excretion of large amounts of uroporphyrin in the urine and stool. It is a chronic, apparently acquired, disorder and typically appears in 50- or 60-year-old males after many years of excessive intake of alcohol. Ingestion of various drugs and chemicals may also precipitate symptoms.[1] Exposure to more than one hepatotoxin probably accelerates and intensifies the hepatotoxic functional disturbances.[2]

Clinically the disease is manifested by cutaneous lesions, (which develop on exposure to heat, light and friction), hirsutism and hyperpigmentation. Diabetes mellitus is present in about one out of three patients, and in 80 to 90 percent of cases there is an abnormal liver function test.[3] A high proportion of patients have significantly elevated serum iron levels, both free and bound.

No curative treatment has been prescribed, but in 1960 Ippen,[4] in Germany described pronounced improvement after repeated venesections. More recently, Epstein and Redeker[5] reported success in reducing symptoms through successive phlebotomies.

Report of a Case

The patient was a 43-year-old white man. Questioning in the course of a routine examination elicited that since a young man he had been subject to numerous blisters on the ears. During the last four to five years he had noticed blisters on the dorsum of both hands, and recently a rash had appeared on the back of his neck. The blistering and rash were aggravated by exposure to the sun, and the lesions persisted. The patient was a heavy consumer of alcoholic beverages and had used them to excess for several years. The only positive physical findings were the extremely fragile blistered hyperpigmented areas covering the posterior neck, dorsum of both hands and the ears.

Hemoglobin, hematocrit, and leukocyte count were within normal limits. Serum iron was in the normal range (96 mcg per 100 ml). Total iron binding capacity (TIBC) was elevated (501 mcg per 100 ml) as was the blood sedimentation rate (40 mm in one hour). There was no indication of facial plethora, polycythemia, siderosis or cirrhosis. Diagnosis of porphyria cutanea tarda was established by the finding of a large amount of porphyrin in the urine (Table 1).

Phlebotomy was performed at approximately two-week intervals, 500 ml of blood being removed each time. A total of 4,600 ml was removed over a period of five months.

Quantitative urine uroporphyrin values were obtained by the Sterling and Redeker method[6] before treatment began and periodically during therapy. Serum iron, TIBC, hemoglobin and hematocrit values were also determined at intervals.

Table 1 shows the patient's progress during the period of phlebotomy. Uroporphyrin values diminished as expected, except for the unusual increase in December 1965. No explanation was found for the temporary reversal in trend.

Four months after the last phlebotomy, the patient was clinically normal, all signs of rash and blistering having disappeared. Hemoglobin and hematocrit values were normal.

The patient continued his alcohol intake unchanged during and after therapy. He was given a follow-up examination 38 months after the last phlebotomy and he was still clinically asympto-

TABLE 1.—*Progress of Phlebotomy Therapy in a Case of Porphyria Cutanea Tarda*

	Ml of Blood Removed	*Urine Uroporphyrin Mcg per Day*	*Hemoglobin Gm per 100 ml*	*Serum Iron Mcg per 100 cc*	*TIBC Mcg per 100 ml*
6/ 7/65	0	8310	13.4	...	...
6/14/65	500	....	...	96	501
6/28/65	500	....	...	...	...
7/12/65	500	....	...	90	286
7/26/65	600	....	...	.	...
8/17/65	500	....	...	70	430
8/30/65	500	....	...	...	...
9/20/65	500	4955	12.3	...	.
10/ 4/65	500	882	12.1	32	384
11/ 8/65	500			63	305
12/ 6/65	0	1725	13.4	105	510
1/20/66	0	230	13.3	200	390
3/10/66	0	.	13.7	163	390
1/25/69	0	2998	13.9	227	341

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matic with no sign of rash or blisters. However, uroporphyrin in the urine had increased significantly, and the serum iron level had risen above the normal limit.

Comment

In this case, repeated venesection therapy carried out over a relatively short time appeared decidedly to alter porphyrin metabolism. The chemical change was accompanied by a remission in clinical signs to the complete elimination of active clinical disease.

Continued absence of symptoms for so extended a period is encouraging, considering that the patient continued to use alcohol. Spontaneous remissions are known to occur in some patients after prolonged abstinence from alcohol.

There is considerable evidence of an association between iron and abnormal porphyrin metabolism in porphyria cutanea tarda. However, Epstein and Redeker[5] noted that increased hepatic iron content is not a prerequisite for response to phlebotomy therapy. Other recent studies[7] indicate that abnormal ferrokinetics with hepatic deposition of iron occur in this disorder, but they do so inconsistently.

Summary

A heavily drinking patient with chemical and clinical evidence of porphyria cutanea tarda was treated by phlebotomy. Removal of 4,600 ml of blood over a five-month period decidedly reduced uroporphyrin excretion with an accompanying remission of the clinical disease, even though the patient did not lessen his intake of alcohol. A follow-up examination after 38 months showed an increase in uroporphyrin excretion but clinical symptoms had not recurred.

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AN INDELIBLE PENCIL FOR ANAL ITCHING

How do you feel about aqueous gentian violet for symptomatic relief of anal pruritis?

"Some years ago a patient came in who had a hot, wet, red bottom; and I wondered whether there was something that I could put on it that would . . . give him a lot of relief. The first thing I saw was an indelible pencil so I painted him with an indelible pencil and told him to use cotton and stop using toilet paper. . . . He came back three days later and said, 'I don't know what you did, but I haven't had any itching since.' So on all of my treatment tables, there's an indelible pencil.

"Now what is an indelible pencil? It's gentian violet, but gentian violet in a higher percentage than you can get in solution (a saturated solution of gentian violet is 2 percent whereas an indelible pencil is about 90 percent. I think it has a binder added). Using dyes like gentian violet is well and good except . . . that you've got to recognize that most of them are alkaline in nature, and you can't use them more than twice a week. If you do, you're going to actually worsen the condition."

—MATTHEW A. LARKIN, M.D., Miami

Extracted from *Audio-Digest General Practice,* Vol. 17, No. 1, in the Audio-Digest Foundation's subscription series of tape-recorded programs.

Congenital Adrenal Cortical Hyperplasia—Successful Long-Term Treatment

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IT IS ALMOST TWO DECADES since Wilkins and coworkers[1] first reported the success of cortisone treatment of the congenital adrenogenital syndrome with adrenal hyperplasia. Since that time the pathophysiology of this syndrome has been delineated and several variants have been described. The subject was thoroughly reviewed recently by Bongiovanni and Root.[2] The number of cases of successful long-term therapy in male children, however, has not been extensive. Experience with such a case, in which the patient was treated with corticosteroids from early childhood for over 15 years, prompts this report.

Report of a Case

The patient was born in January 1952, an apparently normal male, weighing 9 pounds 6½ ounces. Soon after birth intractable vomiting developed and he became dehydrated. He was therefore admitted to Letterman General Hospital at 8 weeks of age with a weight of 7 pounds 5 ounces. Parenteral therapy restored fluid and electrolyte balance, and because of the possibility of congenital hypertrophic pyloric stenosis, celiotomy was performed. No gastrointestinal abnormalities were found; nevertheless a Ramstedt procedure was performed. The patient withstood the surgical operation well. However, when oral feedings were resumed vomiting recurred. At this point, hyponatremia and hyperkalemia were demonstrated and a therapeutic trial of desoxycorticosterone acetate (DOCA) with supplemental sodium chloride was begun. In two days vomiting ceased and body weight stabilized. After two weeks of therapy, DOCA was discontinued. Within 48 hours vomiting recurred. DOCA was given again and the child did well for the remainder of the stay in hospital. Two 24-hour urinary 17-ketosteroid determinations were performed, and both were above normal range at 1.7 and 1.5 mg (normal at this age, 0.1 to 1.0 mg). The patient was discharged 26 May 1952 on a high sodium supplementation and 5 mg of DOCA intramuscularly daily. Six months later the child could be maintained on sodium supplementation without DOCA.

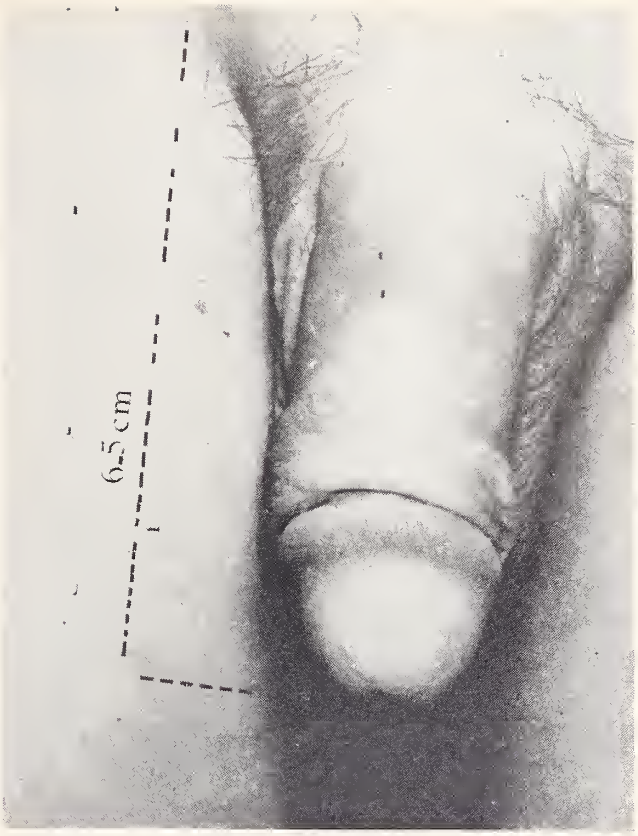

Figure 1.—Secondary sexual development at age 3 years 7 months. Despite the enlarged phallus and pubic hair development, testicular size was normal for the age.

When the patient was 18 months old, the mother first noted rapid growth. Because of the belief it was secondary to the DOCA he had received, it was not until two years later that she brought him to the Letterman Pediatric Clinic for evaluation of precocious growth and development. At that time, the child was 3 years 7 months of age, and he had the appearance of a 6- to 7-year-old child. He had a bone age of 7 to 9 years, a height age of 5½ years (45½ inches tall), pubic hair

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Submitted 27 May 1969.

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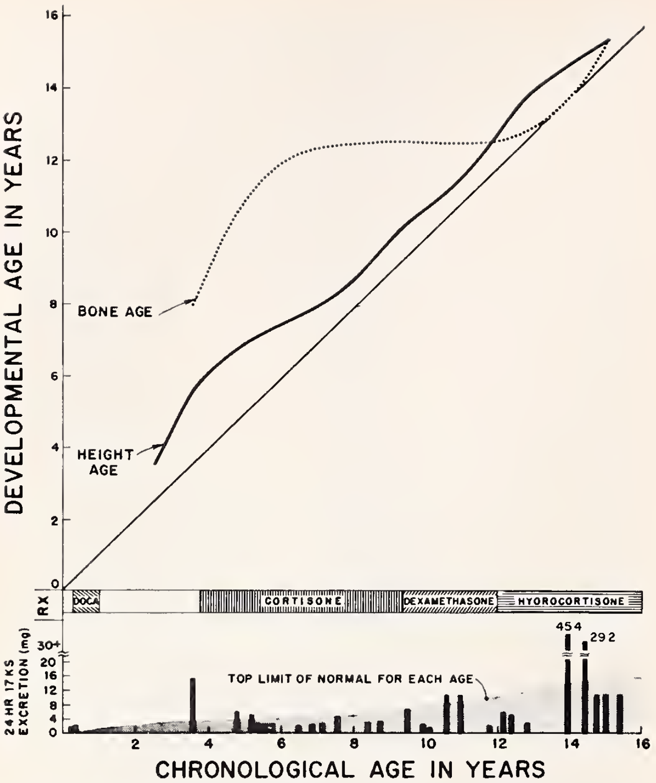

Chart 1.—Effects of treatment on height, bone maturation, and urinary 17-ketosteroid excretion. The relatively low 17-ketosteroid excretion around age 12 occurred when the patient was clinically Cushingoid.

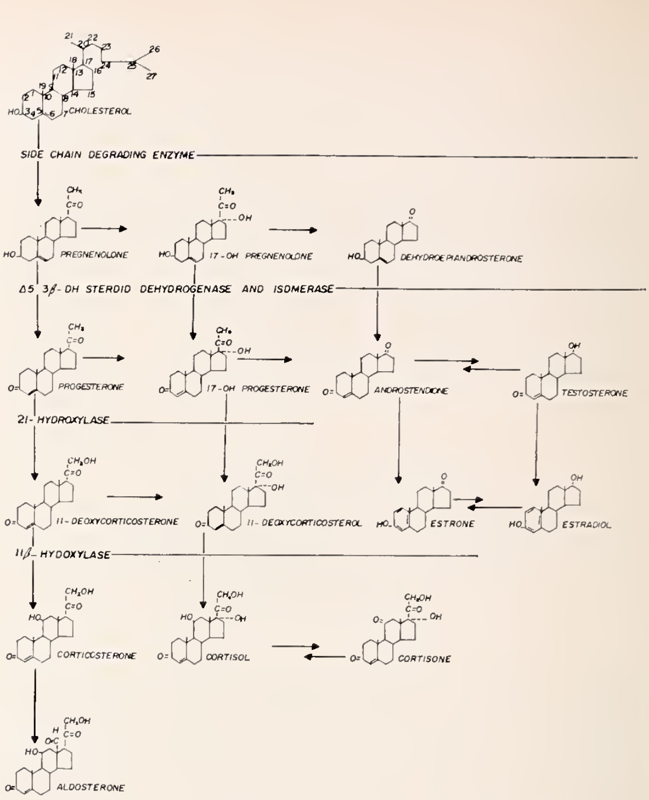

Chart 2.—Sequence of steroid genesis. In the condition reported, a relatively impaired 21-hydroxylation leads to decreased production of mineralocorticoids (including DOCA) and glucocorticoids (including cortisol).

development, and a phallus 6.5 cm in length (Figure 1).

His blood pressure was 80/40 mm of mercury. Urinary 17-ketosteroid excretion was again elevated at 15 mg in 24 hours (normal at this age, 1 to 4 mg). An intravenous pyelogram showed no abnormality, and serum sodium and potassium levels were within normal limits. Chromosome analysis revealed a male genotype. At this time, the patient was first seen by one of the authors. A diagnosis of a congenital adrenogenital syndrome was made and continuous therapy was begun, at first with intramuscular cortisone, later with oral dexamethasone, and then with hydrocortisone. Doses varied over the years from 40 to 75 mg hydrocortisone equivalent daily, the amount depending on urinary 17-ketosteroid excretion patterns and clinical course. The average dose necessary to maintain normal 17-ketosteroid excretion was 60 mg of hydrocortisone per day.

When the patient completed normal puberty and reached a maximal height of 57½ inches and a bone age of 17 years during his sixteenth year, steroid therapy was gradually tapered to discontinuance. Although he remained asymptomatic during this period, endogenous cortisol production did not resume over a nine-month period and replacement therapy with 10 mg of hydrocortisone twice daily was reinstituted. (See Chart 1.)

At no time during the period of corticosteroid therapy had the patient shown evidence of adrenal insufficiency. He had varicella, measles, and a leg fracture without requiring any additional steroids. Except for a period at age 12 when he was receiving 75 mg of hydrocortisone daily and had "over-suppression" of his urinary 17-ketosteroids, clinical signs of Cushing's syndrome were never apparent.

Discussion

Clinically, the history in this case is quite typical of a congenital 21-hydroxylase deficiency. In this condition, a relatively impaired 21-hydroxylation leads to decreased production of mineralocorticoids (including DOCA) and glucocorticoids (including cortisol). (See Chart 2). The patient's mineralocorticoid production was so small that he required exogenous DOCA during his early life, while his decreased cortisol production was manifested later.

Diminished cortisol formation results in increased ACTH stimulation, causing the accumulation of excessive amounts of steroids before the C-21 block. These substances include dehydroepiandrosterone, androstendione and androsterone, which all have potent androgenic potentials. Exogenous corticosteroid therapy serves to inhibit this excessive ACTH secretion and consequently reduces the excessive production of these hormones.

Most of the reported cases of the adrenogenital syndrome have been in females; in one series[3] 78 percent were female. This high proportion, probably does not reflect the true incidence, but the condition is more frequently suspected in females due to their anomalous genitalia at birth. As in the present case, the male's genitalia are normal for the first several months of life. For this reason, male infants with an unrecognized defect may die in infancy from dehydration and circulatory collapse, or from hyperkalemia and cardiac arrest. Frequently, as in the present case, the intractable vomiting leads to a misdiagnosis of hypertrophic pyloric stenosis. Iverson[4] reported a fatal outcome in all of 81 patients who received no specific therapy. Such statistics emphasize the need for awareness of this condition in the male infant with symptoms resembling an Addisonian crisis developing a few weeks after birth. The finding of elevated urinary 17-ketosteroids should confirm the diagnosis.

In the absence of such an early complication, the disease usually goes unrecognized until inordinate growth and maturation become apparent around 2 years of age. At this time, one must consider constitutional precocity and virilizing adrenal tumor in the differential diagnosis. Small testicular size is of help in eliminating the former, and adequate suppression of the elevated 17-ketosteroids upon the administration of cortisol eliminates the latter.

Although the androgen excess is not so critical a problem in the male child as it is in the female in regard to sexual maturation, the effect on acceleration of bone age makes early therapy essential.

The administration of appropriate doses of glucocorticoid hormones may produce gratifying results in prompt deceleration of growth so that ultimate normality can be achieved in height, sexual maturation and fertility. To achieve these good results, the child must be closely monitored with urinary steroid determinations, bone age radiographs, and serum electrolyte studies.

Therapy must be continued indefinitely in children who manifest the salt-losing variety, and in all females. There have been dissenting opinions, however, in regard to whether life-long treatment is necessary in uncomplicated cases in males.[2,5]

It seems most reasonable to us that the relative Addisonian state which most of these patients have is enough reason in itself to advise life-long therapy. The development of an adrenal neoplasm occurring in a patient who has had continuous ACTH excess as the result of the adrenogenital syndrome has been seen in at least one instance.[6] Such a report adds increased impetus to the recommendation for continuous therapy in all cases.

Summary

A case is described of a 16-year-old male with the adrenogenital syndrome with adrenal hyperplasia, due presumably to a 21-hydroxylase deficiency, who has been successfully treated for over 15 years with corticosteroids. The problem of early diagnosis in male infants and the gratifying results of long-term suppressive therapy are emphasized.

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Medical Progress

Chemotherapy Guide

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This review is intended as a guide to proper antimicrobial therapy rather than as an exhaustive, definitive compendium. The outline format was selected to make the material more useful as a ready reference source and to permit early publication, insuring up-to-date data. Much of the presentation requires weighing of one agent against another; every effort has been made to avoid arbitrary or biased interpretations.

The material is organized into sections as follows: sulfonamides (sub-organized into various classes), antibiotics and other antibacterials (arranged in groups, where possible), drugs of choice for specific bacteria, investigational antimicrobial agents (the more promising agents), the use of antibacterial agents in renal insufficiency, and antibiotics and liver disease. Other material which might have been useful (information on antimycobacterial and antiparasitic drugs, principles of antibacterial chemotherapy, additional pharmacologic information, therapy of infectious diseases requiring special regimens, etc.) has been left out in the interest of brevity.

Doses given are for adults. In the presence of impaired renal function, it may be important that dosages be reduced since most antibiotics are principally excreted in the urine. For specific information on this see section "Antibacterial Agents in Renal Insufficiency" by Dr. Ziment.

Superinfections are not mentioned as side effects but may be encountered with any of these agents. They are more likely to occur after the use of "broad-spectrum" agents, which suppress more of the normal flora.

SULFONAMIDES

Sydney M. Finegold, M.D., and Alvin Davis, M.D.

The therapeutic effectiveness of sulfonamides is reduced by pus, necrotic tissue, heavy inocula of organisms and thick fibrin barriers at the periphery of a lesion. Hence, sulfonamide therapy is optimally effective in mild and moderate infections which exhibit minimal suppuration.

I. PRESENT-DAY USES:

A. Urinary infections — chiefly those due to *E. coli*.

B. Meningococcal infections — only if organism known to be sensitive. No longer drugs of choice.

C. *Nocardia* infections—treatment of choice.

D. Bowel surgery — pre- and post-operatively; sulfasuxidine, sulfathalidine.

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Submitted 25 June 1969.

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E. Trachoma, inclusion conjunctivitis — in conjunction with tetracycline.

F. Dermatitis herpetiformis.

G. Rheumatic fever prophylaxis.

H. South American blastomycosis — not as good as amphotericin.

I. Protozoan infections (malaria, toxoplasmosis, *Pneumocystis* infections) — together with pyrimethamine.

J. Glanders, melioidosis.

K. Lymphogranuloma venereum, chancroid.

L. Gastrointestinal tract inflammations — regional enteritis, ulcerative colitis. Intestinal sulfonamides (D above) and Azulfidine.

M. Prevention and treatment of *Pseudomonas* infection of burns (mafenide).

N. Other topical uses—ophthalmic and vaginal.

II. SHORT-ACTING SULFONAMIDES:

A. *Sulfadiazine:*

1. Oral dosage
   - a. 1.0 Gm q 4 h for systemic infections after 3-4 Gm loading dose.
   - b. 0.5 - 1.0 Gm q 6 h for urinary tract infections.
2. Intravenous or subcutaneous use (sodium sulfadiazine) — initial dose of 3-5 Gm in a concentration of 0.5-5.0% in N/S, then 2-3 Gm q 6-12 h.

B. *Triple Sulfa:* Higher solubility than sulfadiazine *in vitro,* but crystalluria may occur. Oral dosage as for sulfadiazine.

C. *Sulfisoxazole (Gantrisin):* Only advantage over sulfadiazine is higher solubility.

1. Dosage—oral—1.0-2.0 Gm q 4-6 h for systemic infections after 3-4 Gm loading dose.
2. Intravenous or intramuscular — Same as oral dosage.

D. *Sulfisomidine (sulfasomidine, sulfadimetine, Elkosin)*:* low acetylation in urine. Useful for urinary infections primarily.

E. *Sulfamethylthiadiazole (sulfamethizole. Thiosulfil)*:* low acetylation, rapid excretion. Useful only for urinary infections.

F. *Sulfachlorpyridazine (Sonilyn)**—Very soluble. Particularly useful for urinary tract infections.

G. *Sulfamethazine (sulphadimidine)* — Used mainly in triple sulfa in U.S.

III. INTERMEDIATE-ACTING SULFONAMIDES: Only advantages are convenience and low cost. Slow excretion may be a disadvantage in the event of a reaction.

A. *Sulfaethidol (Sul-Spansion and Sul-Spantab):* liquid or tablets in sustained release form. Dosage —1-3 Gm (10 ml or 2 tabs) q 12 h.

B. *Sulfamethoxazole (Gantanol):* Resembles sulfisoxazole but is absorbed and excreted more slowly; more likely to cause crystalluria. Dosage 2.0 Gm stat, then 1.0 Gm q 12 h.

C. *Sulfaphenazole (Sulfabid)*—Similar to sulfamethoxazole.

D. *Lipid Suspensions of Sulfonamides:* available for sulfadiazine, triple sulfa, and sulfisoxazole.

IV. LONG-ACTING SULFONAMIDES: These preparations should not be used because of their toxicity.

A. *Sulfamethoxypyridazine (Kynex, Midicel)*

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*Dosage is the same as for sulfadiazine.

B. *Sulfamethoxydiazine (Sulfameter, Sulla)*

C. *Sulfadimethoxine (Madribon)*

D. *Sulphormethoxine*—Very long-acting; therapeutic blood levels for 1 week.

V. POORLY ABSORBED SULFONAMIDES:

for local use in the intestinal tract only.

A. *Succinylsulfathiazole (Sulfasuxidine):*

1. Dosage—3.0 Gm q 4 h p.o.
2. Maximum effect usually not achieved until 7th day of therapy.

B. *Phthalylsulfathiazole (Sulfathalidine):*

1. Dosage—1.5 Gm q 4 h p.o.
2. Double this dosage in the presence of diarrhea.
3. Effect produced in 5-7 days.

C. *Para-nitrosulfathiazole (Nisulfazole):* Used only for intrarectal instillation in treatment of proctitis or non-specific colitis.

VI. TOPICAL SULFONAMIDES:

A. *Mafenide (Sulfamylon):* Used on skin as 10% cream. Unlike other sulfonamides, effective in presence of pus and necrotic tissue and does not sensitize readily when used topically. Of value in prevention and therapy of burn infection due to *Pseudomonas.*

B. *Ophthalmic preparations:* Sodium sulfacetamide (Sulamyd) and sulfisoxazole diolamine are the only products suitable for topical use in the eye; they are available as solutions (30%) and ointments (10%).

C. *Vaginal preparations:* These include sulfisoxazole and triple sulfonamide combinations made up as creams or tablets. They are used in nonspecific vaginitis and cervicitis.

VII. SULFAPYRIDINES:

A. *Sulfapyridine:* Too toxic for general use, but best drug available for dermatitis herpetiformis.

B. *Salicylazosulfapyridine (Azulfidine):* Of value in ulcerative colitis, particularly in preventing relapse. Value in regional enteritis less well established.

VIII. SULFONAMIDES IN GENERAL:

A. Desired peak blood level—8-15 mg/100 ml (except poorly absorbed compounds).

B. Mode of action—bacteriostatic.

IX. TOXICITY AND SIDE EFFECTS:

A. Fever

B. Rash, urticaria

C. Cyanosis, methemoglobinemia

D. Nausea, vomiting, diarrhea

E. Hepatitis, jaundice

F. Hematuria, albuminuria, crystalluria, toxic nephritis.

G. Headache, mental depression, psychosis, peripheral neuritis.

H. Leukopenia, agranulocytosis, purpura, aplastic anemia, hypoprothrombinemia, hemolytic anemia.

I. Severe hypersensitivity reactions — anaphylaxis, periarteritis nodosa and other collagen diseases, Stevens-Johnson syndrome.

X. PRECAUTIONS:

A. Keep careful record of urine output — try to maintain output of at least 1200-1500 ml/24 hrs.

B. Alkalinization of urine—sodium bicarbonate (12-15 Gm/day) may be used for this purpose when full systemic doses of sulfonamides are used, when there is difficulty in being sure of adequate fluid intake and output, and when such adjunctive therapy is not contraindicated.

C. Check fresh urine specimens for RBC's, albumin and sulfa crystals.

D. Weekly blood counts.

ANTIBIOTICS AND ANTIBACTERIALS, GENERAL

Sydney M. Finegold, M.D., and Alvin Davis, M.D.

I. PENICILLIN G (Benzylpenicillin):

1. *Spectrum and Uses:* Highly active against Gram-positive cocci other than beta lactamase-producing staphylococci; Gram-negative cocci; Gram-positive bacilli; fusiforms and some other Gram-negative anaerobic bacilli; and (in high dosage) *Proteus mirabilis.* Oral penicillin G is useful in many urinary tract infections due to *E. coli* and *P. mirabilis.*

2. *Types of Preparations, Route of Administration and Dosage:*

a. *Crystalline aqueous penicillin G:*

(1) Peak blood levels — generally 1-2 units/ml for each one million units intramuscular/day.

(2) Probenecid (Benemid) 0.5 Gm q 6 h will usually raise levels 1½ to 2 times.

b. *Procaine penicillin G suspended in oil or water:*

(1) With single intramuscular dose of 300,000 to 600,000 units, peak serum levels are usually 0.75 unit/ml or less and serum concentrations of at least 0.04 unit/ml (adequate for highly sensitive organisms such as pneumococci and Group A beta-hemolytic streptococci) persist for from 20 to 24 hours. Frequency of administration depends on preparation and dosage used.

(2) Increasing dosage primarily prolongs duration of blood level rather than raising peak level; the usual daily maximum should be 1.2 million units.

c. *Procaine penicillin G in sesame oil and 2% aluminum monostearate:*

A single 200,000 unit dose behaves much like procaine penicillin, but 600,000 unit doses result in levels of 0.03 units/ml or higher for more than 90 hours.

d. *Benzathine penicillin G (dibenzylethylenediamine dipenicillin G, DBED, Bicillin):*

(1) Very insoluble salt. 300,000 unit dose intramuscularly gives levels above 0.03 unit/ml for over 5 days with peak levels above 0.15 unit/ml uncommon at any time. Doses of 600,000 units and 1,200,000 units intramuscularly result in prolongation of levels to 12 and 28 days, respectively. (The oral form is poorly absorbed and should not be used.)

(2) Chiefly useful as a prophylactic agent and in the treatment of early syphilis.

(3) Painful on injection. Allergic reactions, when they occur, may be severe and prolonged.

e. *Oral penicillin G:*

For urinary tract infections, 400,000 units q 6 h.

3. *Toxicity, Side Effects, and Precautions:*

a. Central nervous system toxicity may occur when unusually high doses are used and/or impaired renal function exists.

b. The amount of potassium injected must be considered when very large doses of crystalline aqueous potassium penicillin are used in the presence of impaired renal function. Each 15 million units supplies 975 mg (25 mEq) of potassium.

c. Allergic reactions ranging from minor skin reactions to anaphylactic shock and death occur. The best prophylaxis is a careful history combined with discriminate use of this drug. The usual skin tests and conjunctival tests with penicillin G are unreliable. Use of penicillinase (Neutrapen) for treatment of penicillin allergy should be condemned because there is no proof of its effectiveness and because it may actually increase the hazard.

d. Hemolytic anemia, neutropenia.

4. *Mode of Action:* Bactericidal.

II. ALPHA-PHENOXY-PENICILLINS:*

A. *Phenoxymethyl penicillin (penicillin V, Pen-Vee, V-Cillin):* This compound is better absorbed on oral administration than penicillin G and is more acid stable. The antibiotic spectrum of the two agents is similar. Both are susceptible to staphylococcal beta lactamase. Most infections which will respond to oral therapy can be treated with 250-500 mg q 8 h. Infections such as osteomyelitis or subacute bacterial endocarditis (when they can be treated orally) require >50-1,000 mg q 4-6 h. Penicillin V is not ordinarily useful for therapy of urinary tract infections.

B. *Phenoxyethyl penicillin (phenethicillin, Syncillin, Maxipen, Chemipen, Broxil, Dargil, Alpen):* This compound is very similar to penicillin V.

III. BETA LACTAMASE-RESISTANT PENICILLINS:*

A. *Methicillin (Staphcillin, Celbenin, Dimocillin):*

1. *Spectrum and Uses:* Active vs staphylococci resistant to penicillin G (beta lactamase-producers). Distinctly inferior to penicillin G vs. other organisms.

2. *Routes of Administration and Dosage*

a. Intramuscularly 1 Gm q 3-6 h.

b. Intravenously 1-4 Gm q 4-12 h (12 Gm or more/day in severe infections). It is best given in 50-100 ml over a 30 minute period q 4-6 h. (The drug is relatively unstable, particularly at acid pH's. Make up just before use.)

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*These agents exhibit cross-allergenicity with penicillin G. Probenecid blocks excretion of all penicillins. All are bactericidal.

3. *Toxicity, Side Effects and Precautions*

a. Sensitivity reactions, as with penicillin G.

b. Renal damage (hypersensitivity?) — fever, albuminuria, pyuria, hematuria, oliguria to anuria, nitrogen retention, edema, and eosinophilia may occur. This is apparently reversible, but complete recovery may take months.

c. Bone marrow depression (neutropenia) occurs occasionally.

d. Hemolytic anemia.

e. Each 4 Gm of drug supplies 230 mg (10 mEq) of sodium (drug supplied as sodium salt).

4. *Miscellaneous.* Moderately resistant staphylococci have been isolated rarely. When other agents are to be administred simultaneously, they should be given separately rather than being mixed with the methicillin.

B. *Oxacillin (Prostaphlin, Resistopen):*

1. *Spectrum and Uses:* Similar to methicillin, but somewhat more active on a weight basis. There is greater protein binding with this agent.

2. *Routes of Administration and Dosage:*

a. Oral—not recommended (cloxacillin or dicloxacillin are preferred oral agents.

b. Intramuscularly—0.5-1.0 Gm q 4 h.

c. Intravenously—0.5 Gm or more q 4 h. May be administered by method described for methicillin.

3. *Toxicity, Side Effects and Precautions:*

a. Sensitivity reactions as with penicillin G.

b. Neutropenia (rare).

c. Reversible SGOT elevations are occasionally noted.

4. *Miscellaneous* — cross-resistance with methicillin. Greater amount of biliary excretion than with methicillin. Not suitable for treatment of meningitis.

C. *Cloxacillin (Tegopen):*

1. *Spectrum and Uses:* Same as for oxacillin.

2. *Routes of Administration and Dosage:* Available only for oral use. Dosage is 0.5-1.0 Gm q 6 h.

3. *Toxicity, Side Effects and Precautions:*

a. Same as for oxacillin.

b. Nausea, epigastric distress, diarrhea, bitter taste.

4. *Miscellaneous:* Preferred over oral oxacillin because of better absorption and thus higher and more prolonged blood levels. Not suitable for treatment of meningitis.

D. *Dicloxacillin (Dynapen, Veracillin):*

1. *Spectrum and Uses:* Same as for oxacillin.

2. *Routes of Administration and Dosage:* Available only for oral use. Dosage is 0.25-1.0 Gm q 6 h.

3. *Toxicity, Side Effects and Precautions:* Same as for cloxacillin.

4. *Miscellaneous:* Peak serum levels approximately twice those with cloxacillin at comparable dosage.

E. *Nafcillin (Unipen):*

1. *Spectrum and Uses:* Similar to oxacillin.

2. *Routes of Administration and Dosage:*

a. Oral—absorption not reliable.

b. Intramuscularly—0.5 Gm q 4-6 h.

c. Intravenously—0.5-1.0 Gm q 4 h. May be administered by method described for methicillin.

3. *Toxicity, Side Effects and Precautions:* As with oxacillin.

4. *Miscellaneous* — Significant biliary excretion.

IV. BROAD-SPECTRUM PENICILLINS:*

A. *Ampicillin (Penbritin, Polycillin):*

1. *Spectrum and Uses:*

a. Active vs most strains of *Proteus mirabilis* and occasional strains of other *Proteus* species. Active vs most strains of *H. influenzae, Salmonella* and *Shigella,* and about 50% of *E. coli* strains.

b. Similar to penicillin G in its activity vs Gram-positive cocci and vs anaerobes except that it is more effective vs many strains of enterococcus.

c. Susceptible to action of beta lactamase and therefore not effective vs most strains of *S. aureus.*

2. *Routes of Administration and Dosage:*

a. Oral—0.5-1.0 Gm q 4-6 h (probably best given one-half hour to an hour before meals).

b. Intramuscularly—0.5-1.0 Gm q 4-6 h.

c. Intravenously — 1.0-2.0 Gm or more

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*These agents exhibit cross-allergenicity with penicillin G. Probenecid blocks excretion of all penicillins. All are bactericidal.

q 4 h; may be administered in the same way as recommended for methicillin.

3. *Toxicity, Side Effects and Precautions:*

a. Sensitivity reactions as with penicillin G.

b. Bone marrow depression.

c. SGOT elevation (occasional).

d. Diarrhea (may be fulminant).

e. Moniliasis and other superinfections are more frequent than with other (narrower spectrum) penicillins.

4. *Miscellaneous* — Significant biliary excretion.

V. CEPHALOSPORINS:

A. *Cephalothin (Keflin):*

1. *Spectrum and Uses:*

a. Active vs most strains of *P. mirabilis* and some strains of other *Proteus* species and vs most strains of *Salmonella* and *Shigella.* Active vs approximately 50% of strains of *Klebsiella-Enterobacter* and *E. coli.* It is not particularly active vs *H. influenzae.*

b. Similar to penicillin G in its activity vs Gram-positive cocci other than *S. aureus* but less active vs pneumococci. It is less active vs most anaerobes.

c. Resistant to beta lactamase and therefore effective vs penicillin-resistant *S. aureus.*

2. *Routes of Administration and Dosage:* Not acid-stable; must be given parenterally.

a. Intramuscularly—0.5 Gm q 6 h for average case. Up to 1.0 Gm q 4 h in severe or relatively resistant infections.

b. Intravenously—0.5 Gm q 6 h to 2.0 Gm q 3 h or more. May be administered by method described for methicillin.

3. *Toxicity, Side Effects and Precautions:*

a. Probably cross-allergenic with penicillins. Same type of side effects as with penicillins.

b. SGOT elevation (occasional).

c. Superinfections, particularly with *Pseudomonas.*

4. *Mode of Action*—bactericidal.

B. *Cephaloridine (Loridine):*

1. *Spectrum and Uses:*

a. Essentially the same as for cephalothin, except that it is more active against susceptible anaerobic organisms than is cephalothin.

2. *Routes of Administration and Dosage:* available only for parenteral use.

a. Intramuscularly — 0.5-1.0 Gm q 6 h. Approved use of drug at the time of this writing restricts maximum daily dose to 4 Gm/day.

b. Intravenously—0.5-1 Gm q 6 h. May be administered by method described for methicillin. Maximum approved dose by this route is 4 Gm/day as well.

3. *Toxicity, Side Effects and Precautions:*

a. Nephrotoxicity has occurred when drug is administered in doses in excess of 4 Gm/day. This has usually occurred in patients with impaired renal function. However, all patients treated with this drug should be observed carefully and frequent urinalysis and serum creatinine levels should be obtained. This drug should not be used in patients with impaired renal function.

b. Cross allergenicity with cephalothin and possibly with penicillins as well.

c. Hematologic abnormalities — transient leukopenia, eosinophilia, hemolytic anemia (rare).

d. Superinfections, particularly *Pseudomonas.*

4. *Mode of Action*—bactericidal.

VI. STREPTOMYCIN:

1. *Spectrum and Uses:* Should never be used alone because of extremely rapid development of resistance by various bacteria. In combination with other agents, this drug is useful in tuberculosis, enterococcal infections, in endocarditis due to various organisms, in granuloma inguinale, and in *Pasteurella* infections.

2. *Routes of Administration and Dosage:* Intramuscularly—0.5-1.0 Gm q 12 h to 1.0 Gm 2-3 times weekly.

3. *Peak Blood Levels:* 20-40 mcg/ml after dose of 0.5-1.0 Gm.

4. *Toxicity, Side Effects and Precautions:*

a. Dermatitis (may be severe), drug fever.

b. Nephrotoxicity.

c. VIII nerve damage — primarily vestibular.

d. Bone marrow depression (uncommon).

e. Intraperitoneal, intrapleural, or rapid intravenous administration, particularly in association with ether anesthesia, may result in curare-like effect with respiratory paralysis. Neostigmine is the antidote of choice.

5. *Mode of Action:* Bactericidal.

VII. TETRACYCLINES:

1. *Spectrum and Uses:* Active against many Gram-positive and Gram-negative bacteria, vs rickettsiae, *Mycoplasma* and *Chlamydia* (Bedsonia). Most *S. aureus* are resistant. Twenty percent of Group A beta-streptococci are resistant, and occasional pneumococci are resistant.

2. *Routes of Administration and Dosage:*

a. Oral—

(1) Tetracycline, oxytetracycline, and chlortetracycline—250-500 mg q 6 h.

(2) Demethylchlortetracycline and methacycline—150 mg q 6 h or 300 mg q 12 h.

(3) Doxycycline—100 mg q 12 h x 3 doses, then 100 mg daily.

b. Intramuscularly—

(1) Tetracycline and oxytetracycline — 100 mg q 8-12 h.

(2) Rolitetracycline—350-700 mg daily in 1 or 2 injections.

c. Intravenously—

(1) Tetracycline, oxytetracycline, and chlortetracycline—500 mg q 8-12 h (by slow drip only).

(2) Rolitetracycline—350-700 mg q 12 h (over 15-30 minute period).

3. *Peak Blood Levels:*

a. Oral or Intramuscular—0.5-3.0 mcg/ml.

b. Intravenous—8-10 mcg/ml.

4. *Toxicity, Side Effects, and Precautions:*

a. Oral.

(1) Nausea, vomiting, anorexia, epigastric distress.

(2) Diarrhea, flatulence, proctitis.

(3) Stomatitis, glossitis.

(4) Dermatitis.

(5) Accumulation in teeth and bones — may cause pigmentation and enamel defects in teeth of children.

(6) Anaphylactoid reactions (rare).

(7) Phototoxic reactions (more common with DMCT).

(8) Vaginitis.

b. Intramuscular—local pain.

c. Intravenous.

(1) Thrombophlebitis

(2) Hepatotoxicity may be seen with daily doses exceeding 1.5 grams. With intravenous usage this may be accentuated (or found at lower dose levels) in the presence of impaired kidney function and/or pregnancy.

d. DMCT—May show, in addition to items listed above in 4. a, nephrogenic diabetes insipidus.

e. Special toxicity in the presence of impaired renal function (may be delayed).

(1) Increasing azotemia, acidosis, hyperphosphatemia.

(2) Anorexia, nausea, emesis.

(3) Weight loss.

(4) Increased urinary losses of nitrogen and sodium.

These effects may be avoided by reduced dosage. They are reversible. Anabolic steroids may prevent or retard these effects also.

f. Special toxicity with outdated drug—Fanconi syndrome may occur (reversible).

5. *Mode of Action:* Bacteriostatic.

6. *Miscellaneous:* The antibacterial activity of tetracycline is counteracted by certain multivalent metallic ions. Therefore, it is best to avoid concurrent administration of such things as aluminum hydroxide gel, milk, etc.

7. *Types of Tetracycline Preparations Available:*

a. Tetracycline (Achromycin, Cosa-tetracyn, Panmycin, Polycycline, Steclin, Sumycin, Tetracyn, Tetrex).

b. Oxytetracycline (Terramycin).

c. Chlortetracycline (Aureomycin).

d. Demethylchlortetracycline (Declomycin, DMCT).

e. Methacycline (Rondomycin).

f. Doxycycline (Vibramycin).

g. Rolitetracycline (Syntetrin, Velacycline).

These drugs are very similar chemically and biologically. There may be some quantitative differences in antibacterial activity against certain species or strains; oxytetracycline seems to be generally superior to the others against *Pseudomonas*. There is virtually complete cross-resistance between the various agents.

VIII. CHLORAMPHENICOL (Chloromycetin)

1. *Spectrum and Uses:* Active against many Gram-positive and Gram-negative bacteria, rickettsiae and *Chlamydia* (Bedsonia). Best drug for typhoid fever. In a number of localities, signficant numbers of staphylococci are resistant.

2. *Routes of Administration and Dosages:*

a. Oral—0.5 Gm q 6 h. Occasionally higher dosages are indicated.

b. Intramuscular—Must not be used by this route; absorption not dependable.

c. Intravenous — Chloramphenicol succinate 0.5 Gm q 4-6 h, each dose administered in 50 ml *over 15 minute period.*

3. *Peak Blood Levels:* 10-20 mcg/ml, by any of above routes.

4. *Toxicity, Side Effects and Precautions:*

a. Bone marrow depression (any or all elements); may be fatal. In rare instances, there is idiosyncratic bone marrow depression unrelated to dosage; apparently more common in white female children and after multiple courses. In most patients, however, toxicity is well correlated with dosage and blood levels and with duration of treatment. Elevation of serum iron and drop in reticulocyte count are early signs of toxicity. Complete blood counts should always be done at regular intervals.

b. "Gray syndrome" in premature and neonatal infants.

c. Optic or peripheral neuritis (rare).

5. *Mode of Action:* Primarily bacteriostatic.

6. *Miscellaneous:* There may be a greater hazard of toxicity in patients with impaired liver function. Biliary excretion is poor.

IX. MACROLIDES:

A. *Erythromycin (Erythrocin, Ilosone, Ilotycin):*

1. *Spectrum and Uses:* Active against Gram-positive organisms primarily. Fifteen percent or more of *S. aureus* strains are resistant in some areas. Usefulness in staphylococcal infections (as a single agent) limited by initial resistance or development of resistance. Also useful in *Hemophilus* and *Mycoplasma* infections.

2. *Routes of Administration and Dosage:*

a. Oral or Intravenous—0.5 Gm q 6 h.

b. Intramuscular — 100 mg q 8-12 h. Give *deep* intramuscularly.

3. *Peak Blood Levels:*

a. Erythromycin base or stearate (Ilotycin, Erythrocin) 0.5-3.0 mcg/ml.

b. Erythromycin estolate (propionyl erythromycin lauryl sulfate, Ilosone)—Levels 2-3 times those with erythromycin base or stearate and more consistent. This compound is available only for oral administration.

4. *Toxicity, Side Effects, and Precautions:*

a. Diarrhea, occasional nausea and vomiting.

b. Mild rash (infrequent).

c. Anaphylaxis (rare).

d. Intrahepatic cholestasis with jaundice is seen occasionally in patients on erythromycin estolate. Eosinophilia (in the peripheral blood) occurs with this. The syndrome is a hypersensitivity phenomenon, occurring typically when the drug is taken for 10 days or more or in repeated courses. The symptoms may recur, in sensitive patients given another course, within 48 hours or even after a single dose.

e. Intramucular injection usually *very* painful.

5. *Mode of Action:* Bacteriostatic

B. *Oleandomycin, triacetyloleandomycin (Cyclamycin, Matromycin, TAO):*

These agents have similar activity and there is marked cross-resistance between them and erythromycin as well. Erythromycin is significantly more active than these drugs and since resistance develops relatively easily to any of these agents, the other agents should not be used except under very unusual circumstances where it is demonstrated that an organism is sensitive to one of them and not to erythromycin and another better agent is not available.

Both intrahepatic cholestasis and hepatocellular abnormality occur with triacetyloleandomycin; a significant percentage of patients receiving 1 Gm/day for over two weeks may show such changes. Oleandomycin shows little toxicity.

X. LINCOMYCIN (Lincocin):

1. *Spectrum and Uses:* Active against Gram-positive coccal organisms (including most strains of *S. aureus*) and anaerobes (with the exception of *Bacteroides fragilis*). No activity against *H. influenzae*. Moderate activity vs. *Mycoplasma.*

2. *Routes of Administration and Dosage:*

a. Oral—0.5-1.0 Gm q 6 h.

b. Intramuscular—600 mg q 12 h.

c. Intravenous—600 mg q 6-8 h.

3. *Peak Blood Levels:*

a. Oral—3-5 mcg/ml

b. Parenteral—6-13 mcg/ml.

4. *Toxicity and Side Effects:*

a. Diarrhea.

b. Occasional nausea, emesis or abdominal distress.

c. Occasional rash or urticaria.

d. Local reactions to intramuscular injection (inflammation).

e. Neutropenia—rare, reversible.

f. Abnormal SGOT levels (occasional).

5. *Miscellaneous:* One-way cross-resistance with erythromycin; strains of *S. aureus* resistant to lincomycin are also resistant to erythromycin.

XI. NOVOBIOCIN (Albamycin):

1. *Spectrum and Uses:* Sometimes useful in *Proteus* (particularly *P. mirabilis* and *P. vulgaris)* infections. Should not be used for pneumococcal or streptococcal infections. Rarely of use in treatment of staphylococcal infections at the present time.

2. *Routes of Administration and Dosage:*

a. Oral—0.25 to 0.5 Gm q 6 h or 0.5-1.0 Gm q 12 h.

b. Intramuscular or intravenous — Same as for oral. *Incompatible with dextrose-containing solutions.* Give slowly intravenously.

3. *Peak Blood Levels:* 20-40 mcg/ml; considerable protein binding.

4. *Toxicity, Side Effects, and Precautions:*

a. Neutropenia—typically mild and reversible. Pancytopenia reported rarely. Hemolytic anemia—rare.

b. Rashes — incidence 10-20%. Occur after 7th to 9th day. May be readily managed with antihistamines as a rule.

c. Urticaria, drug fever, eosinophilia.

d. Appearance of a yellow pigment in the plasma (which may interfere with the determination of serum bilirubin and icteric index) may mask evidence of true liver damage and is therefore an indication for discontinuing the drug.

e. In neonates and young infants, there may be interference with conjugation of bilirubin.

5. *Mode of Action:* Usually bacteriostatic.

6. *Miscellaneous:* There is relatively poor distribution in tissues.

XII. KANAMYCIN - NEOMYCIN - PAROMOMYCIN GROUP:

A. *Kanamycin (Kantrex):*

1. *Spectrum and Uses:* Safest of group for parenteral administration. Poorly absorbed orally; oral usage is for intestinal infections or for "bowel sterilization." Very effective against a wide variety of Gram-positive and Gram-negative organisms. Ineffective, or relatively so, against *Pseudomonas,* streptococci, pneumococci, anaerobes, *Brucella.* Some Klebsiella-Aerobacter strains are resistant. A significant number of *S. aureus* strains at many institutions are extremely resistant. This resistance is high enough to exceed concentrations of drug used topically or achieved in G.I. tract after oral administration.

2. *Routes of Administration and Dosage:*

a. Intramuscular — 15 mg/kg/day or less (usually 1 Gm/day or less). Divided into 2-4 doses.

b. Intravenous — same as intramuscular. Give very slowly. Avoid this route entirely, if possible, particularly in presence of impaired renal function.

c. Oral—1.5 Gm q 4-6 h. Loading dose of 1.0 Gm q h x 4 may be used when rapid effect is desired. Some workers prefer to never exceed 4.0 Gm/day orally.

3. *Peak Blood Levels:*

a. Parenteral—20-35 mcg/ml.

b. Oral—negligible except with severe hepatic disease, renal disease, or in the presence of extensive bowel ulceration.

4. *Toxicity, Side Effects, and Precautions:*

a. Nephrotoxicity—azotemia is chief manifestation. Seen more often in patients with pre-existing impairment of renal function. Recovery slow (4-6 weeks) but apparently complete as judged by the usual clinical determinations. Seen in older patients in absence of obvious evidence of pre-existing impaired renal function.

b. Ototoxicity — both branches of VIII nerve may be involved, but primarily the auditory. Related to dosage, blood level, duration of therapy, impaired renal function (pre-existing or caused by drug), and previous perceptive hearing loss. May occur even with oral therapy in patients with poor renal function, etc. More likely to occur with concomitant or *sequential* use of other ototoxic agents. Essentially irreversible. Observe patients closely for such early evidences of ototoxicity as tinnitus, "fullness" in the ear, and/or audiometric evidence of loss of acuity. Loss of acuity at 4000 and 8000 cycles typically occurs before subjective hearing loss.

c. Pain at injection site occasionally—usually prevented by procaine.

d. Curare-like effect with respiratory paralysis or arrest—may follow intraperitoneal, intrapleural, or rapid intravenous administration, particularly in association with ether anesthesia. Calcium gluconate or neostigmine should be tried as antidotes.

e. Since kanamycin is dialyzable, consideration should be given to utilizing dialysis promptly in patients with early evidence of toxicity.

B. *Gentamicin (Garamycin):*

1. *Spectrum and Uses:* Active against most Gram-negative bacteria including *E. coli, Pseudomonas aeruginosa* and *Proteus* species. Kanamycin is more active against *Proteus* species and some strains of Klebsiella-Enterobacter but gentamicin is effective against some strains of Klebsiella-Enterobacter which are resistant to kanamycin. It is the drug of choice for serious *Pseudomonas* infections, recognizing that occasional strains may be resistant. Its role in the management of staphylococcal infection remains to be defined. It is ineffective against streptococci, pneumococci, and anaerobes.

2. *Routes of Administration and Dosage:*

a. Intramuscular—0.4-1.0 mg/kg q 8 h. In serious infections, doses of 1.5 mg/kg q 8 h have been used for limited periods.

b. Topical.

3. *Peak Blood Levels:* With normal renal function, doses indicated do not usually produce serum levels in excess of 10 mcg/ml.

4. *Toxicity, Side Effects, and Precautions:*

a. Similar to that indicated for kanamycin.

b. Ototoxicity — both branches of VIII nerve may be involved, but the vestibular branch is involved more often. Predisposing factors as described under kanamycin probably apply to this drug as well.

C. *Neomycin (Mycifradin):*

1. *Spectrum and Uses:* Very similar to kanamycin. Should not be used parenterally because of greater toxicity. Cross-resistance with other members of group may be seen.

2. *Routes of Administration and Dosage:*

a. Oral—as with kanamycin.

b. Topical—5 mg/ml or Gm. Caution: large volumes of irrigating fluid or prolonged administration may produce enough absorption to cause toxicity.

3. *Peak Blood Levels:*

Oral — negligible, except in patients with severe hepatic failure, renal disease, or extensive bowel ulceration.

4. *Toxicity, Side Effects, and Precautions:* Qualitatively similar to kanamycin, but more toxic. Here, neostigmine is probably antidote of choice for neuromuscular block. Deafness may progress for extended periods after therapy has been stopped and blood levels are no longer demonstrable.

5. *Mode of Action:* Bactericidal.

D. *Paromomycin (Humatin):*

Similar to kanamycin and neomycin and shows cross-resistance with them. Used only orally. May be more effective in intestinal amebiasis than related compounds.

XIII. POLYMYXIN-COLISTIN GROUP:

A. *Polymyxin B Sulfate (Aerosporin):*

1. *Spectrum and Uses:* Effective vs. most Gram-negative bacilli other than *Proteus.* Diffuses poorly into body cavities and tissues. Susceptible to inactivation by constituents of cells and tissues. Orally, there is very little absorption so it is useful for some enteric infections.

2. *Routes of Administration and Dosage:*

a. Intramuscular — 2.5 mg/kg body weight/day; give in 3 divided doses (q 8 h). Average dosage is 50 mg q 8 h intramuscularly. May be diluted with procaine.

b. Oral — 10-20 mg/kg/day, divided into 4 doses (not absorbed).

c. Intravenous—Same dosage as intramuscular, but never over 200 mg per day. Administer each dose over 60 to 90 minute period.

d. Topical—0.1 to 0.25% concentration.

e. Intrathecal — Treatment of choice for *Pseudomonas* meningitis. 5-10 mg in 10 ml of N/S first day, then 5 mg daily for 3 days, then 5 mg every other day.

3. *Peak Blood Levels:* About 2 mcg/ml.

4. *Toxicity, Side Effects, and Precautions:*

a. Nephrotoxicity; rising creatinine is indication for lowering dosage or discontinuing drug. Renal shutdown rare. Changes usually reversible, as far as is known.

b. Neurotoxicity — Paresthesias, ataxia, weakness of legs, dizziness. Entirely reversible, but may be disturbing enough to patient to force cessation of treatment.

c. Very painful on injection for most patients.

d. Drug fever.

e. The possibility of neuromuscular blockade with respiratory paralysis should be kept in mind when this agent is used intraperitoneally, intrapleurally, or intravenously. Calcium gluconate counteracts this effect experimentally.

B. *Colistin methanesulfonate (Coly-Mycin):* Similar to polymyxin B. Should not be used intravenously or intrathecally (contains dibucaine). Intramuscular dosage—5.0 mg/kg per day in divided doses (q 6 h). Much less pain at intramuscular injection sites. (However, polymyxin given intravenously avoids this problem.) Toxicity comparable to polymyxin B when both are used at full therapeutic dosage. Currently more expensive than polymyxin B.

XIV. VANCOMYCIN (Vancocin):

1. *Spectrum and Uses:* Active against essentially all Gram-positive organisms; ordinarily should be reserved for infections not readily treatable with less toxic agents.

2. *Routes of Administration and Dosage:*

a. Oral — 4 grams/day. Absorption negligible, so useful only for staphylococcal enterocolitis.

b. Intravenous — Parenteral administration must be by the intravenous route. Dosage—2 Gm daily, preferably 1 Gm q 12 h in volume of 50-100 ml administered over 15-30 minutes.

3. *Peak Blood Levels:* 5-20 mcg/ml.

4. *Toxicity, Side Effects, and Precautions:*

a. Thrombophlebitis — less common when given intermittently rather than by constant intravenous drip.

b. Rash, urticaria, drug fever.

c. Anaphylactoid reactions—rare.

d. Nephrotoxicity — particularly in patients with previous impairment of renal function.

e. Ototoxicity—much less frequent than with kanamycin. Related to high blood levels, whether due to impaired renal function or not.

f. Leukopenia (rare).

5. *Mode of Action:* Bactericidal.

6. *Miscellaneous:* It appears to be very difficult to induce resistance to this drug either *in vitro* or *in vivo*.

XV. BACITRACIN:

1. *Spectrum and Uses:* Active against Gram-positive organisms primarily. Rarely used parenterally at present.

2. *Routes of Administration and Dosage:*

a. Parenteral — 50,000 to 100,000 units daily, divided into 4 doses (q 6 h) intramuscularly. Should be diluted in procaine in normal saline. Give *deep* intramuscularly.

b. Intrathecal — 5,000 to 10,000 units in normal saline daily (for staphylococcal meningitis). Very well tolerated by CNS.

c. Topical—500 to 1,000 units/ml or Gm.

3. *Peak blood levels* after parenteral use—0.3 to 3.0 units/ml.

4. *Toxicity, Side Effects, and Precautions:*

a. Pain at injection site.

b. Nephrotoxicity — renal tubular necrosis may occur. If patient's blood urea nitrogen or creatinine is normal and remains so, toxicity will usually be minimal and reversible. Watch urinary output carefully.

5. *Mode of Action:* Bactericidal.

XVI. NITROFURANS:

A. *Nitrofurantoin (Furadantin)*

1. *Spectrum and Uses:* Useful only for urinary tract infections. Most urinary tract infections with *E. coli,* staphylococci and enterococci respond. About 50% of infections due to *Proteus* species or Klebsiella-Enterobacter respond. *Pseudomonas* is resistant and may cause superinfection.

2. *Routes of Administration and Dosage:*

a. Oral—50-100 mg q 6 h.

b. Intravenous (Furadantin sodium)—180 mg in 500 ml of diluent q 12 h (60 drops/minute). Reduce dosage for patients under 120 lbs. Dissolve crystals just prior to use.

3. *Blood Levels:* Negligible.

4. *Toxicity, Side Effects, and Precautions:*

a. Nausea, vomiting—minimized by taking drug with food.

b. Headache, malaise, dizziness.

c. Rash, urticaria, other sensitivity reactions (including pulmonary infiltrates).

d. Hemolytic anemia in certain susceptible patients (people with red cells having glucose-6-phosphate dehydrogenase deficiency).

e. Peripheral neuritis — particularly in patients with impaired renal function or predisposition to neuritis (diabetes, avitaminosis, etc.).

5. *Mode of Action:* Primarily bacteriostatic.

6. *Miscellaneous:* Macrodantin is a macrocrystalline form of nitrofurantoin which is probably comparable in activity and which may offer the advantage of fewer gastrointestinal side effects.

B. *Furazolidone (Furoxone):*

1. *Spectrum and Uses:* This nitrofuran is used for treatment of enteric disease due to *Shigella* and *Giardia.*

2. *Route of Administration and Dosage:* 100 mgm orally q 6 h.

3. *Toxicity, Side Effects, and Precautions:*

a. Reactions similar to those described for nitrofurantoin.

b. Disulfiram-like reactions may occur after alcohol in patients on this drug.

c. Urine may turn brown (not a sign of toxicity).

4. *Blood Levels:* Drug absorbed poorly; blood levels very low.

XVII. NALIDIXIC ACID (NegGram):

1. *Spectrum and Uses:* Useful primarily for urinary tract infections. May be useful in therapy of *Shigella* and enteropathogenic *E. coli* enteritis and the *Salmonella* carrier state, but available studies are not adequate to allow one to properly judge its place in the management of these conditions. In the case of urinary tract infection, it is most useful against *Proteus* but may also be useful in infections due to *E. coli,* Klebsiella-Enterobacter and occasionaly strains of *Pseudomonas,* staphylococci and enterococci.

2. *Routes of Administration and Dosage:* Available only for oral use. The usual initial dose is 4.0 Gm/day given in four divided doses. If therapy is continued for longer than 7-10 days, dosage should be reduced to 2.0 Gm/day.

3. *Toxicity, Side Effects, and Precautions:*

a. Nausea, emesis, occasionally diarrhea.

b. Rash, urticaria, drug fever, eosinophilia, photosensitivity.

c. Occasional elevation of SGOT.

d. Occasional neural disturbances — headache, drowsiness, dizziness, visual disturbances, acute toxic psychosis, convulsions.

XVIII. AMPHOTERICIN B (Fungizone):

1. *Spectrum and Uses:* Effective against both North and South American blastomycosis, histoplasmosis, moniliasis, sporotrichosis, cryptococcosis (torulosis), aspergillosis, mucormycosis and coccidioidomycosis.

2. *Routes of Administration and Dosage:*

a. Intravenous — Start with daily dose of 5 mg and increase gradually (by 5-10 mg/day) to maintain dosage of 50-70 mg every other day. Drug must be administered in 5% dextrose *in water* using 100 to 150 ml of solution for each 10 mg of drug. Administer over not less than 6 hour period, using small gauge needle. Analgesics, antihistamines, sedatives, etc. may be used to minimize reactions. Total dosage should not exceed 2.0-3.0 Gm, if possible.

b. Intrathecal or intraventricular* — Dilute drug in sterile distilled *water* to a concentration of 0.25 mg/ml. The initial dose should not exceed 0.1 mg. This should be administered slowly after first diluting solution with 6-8 volumes of spinal fluid. Increase dosage at rate of 0.1 mg for each subsequent injection to maximum of 0.5-0.7 mg. Solutions must be made fresh each time. Injections should be given 3-4 x weekly, preferably alternating between lumbar and cisternal sites after the first few lumbar injections. Ordinarily, this schedule is followed for approximately one month and then maintenance injections of 0.5 mg are given intracisternally once weekly for at least two more months. Intraventricular therapy may be used in place of lumbar or cisternal intrathecal therapy.

c. Topical—Amphotericin may also be used locally in the pleural space, joints, directly into superficial lesions, etc., in selected cases.

3. *Toxicity, Side Effects, and Precautions:*

a. Fever, chills, headache, nausea, vomiting.

b. Phlebitis.

c. Anemia; requires transfusion at times.

d. Nephrotoxicity—Unique nephropathy involving hyperkaluria, nephrocalcinosis and other features suggestive of renal tubular acidosis. Decreased glomerular perfusion is another feature. Renal toxicity probably best followed by endogenous creatinine clearance.

e. Arachnoiditis may follow intrathecal therapy.

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*Repeated intraventricular injection is feasible only when a device such as an Ommaya valve has been implanted surgically.

DRUGS OF CHOICE FOR SPECIFIC BACTERIA

Sydney M. Finegold, M.D., and Alvin Davis, M.D.

The choices below are not necessarily appropriate for urinary tract infection. See sections on sulfonamides, oral penicillin G, nitrofurantoin and nalidixic acid for information concerning the use of these agents in urinary tract infections.

All the drugs effective against a given organism are not necessarily listed. Drugs listed first are usually the most effective or least toxic, or both. Italicized drugs are outstanding in effectiveness against the particular organism.

GRAM-NEGATIVE BACILLI

Organism	*Drug of Choice*
Achromobacter anitratus	Kanamycin, polymyxin or colistin, tetracycline, erythromycin
Achromobacter lwoffii	Tetracycline, kanamycin, polymyxin or colistin, erythromycin, chloramphenicol
Achromobacter—other species	Polymyxin or colistin, kanamycin, tetracycline, chloramphenicol
Actinobacillus actinomycetemcomitans	Tetracycline, streptomycin, chloramphenicol, ? ampicillin, ? penicillin
Actinobacillus lignieresii	Kanamycin, ? polymyxin or colistin
Aeromonas hydrophila	Tetracycline, kanamycin, chloramphenicol
Arizona	Ampicillin, cephalothin, tetracycline, chloramphenicol
Bacteroides fragilis	Tetracycline, chloramphenicol, erythromycin, lincomycin, penicillin
Bacteroides melaninogenicus	*Penicillin,* linomycin, tetracycline, chloramphenicol
Bartonella bacilliformis	Penicillin C, chloramphenicol, streptomycin, tetracycline
Bordetella pertussis	Ampicillin, tetracycline
Brucella	Tetracycline, chloramphenicol
Calymmatobacterium granulomatis	Tetracycline, streptomycin, chloramphenicol
Chromobacterium	Streptomycin, tetracycline, chloramphenicol
Citrobacter	Polymyxin or colistin, kanamycin, chloramphenicol, tetracycline
E. coli	Chloramphenicol, tetracycline, kanamycin, gentamicin, ampicillin, cephalothin, polymyxin
Edwardsiella	Tetracycline, chloramphenicol, polymyxin or colistin, ampicillin
Enterobacter — Subgroup A (Aerobacter cloacae)	Gentamicin, kanamycin, polymyxin or colistin
Enterobacter — Subgroup B (Aerobacter aerogenes)	
Enterobacter — Subgroup C (Aerobacter liquefaciens)	
Flavobacterium	Chloramphenicol, sulfadiazine
Fusobacterium (fusiform bacilli)	*Penicillin,* lincomycin, tetracycline, chloramphenicol
Hafnia	Tetracycline, chloramphenicol, kanamycin
Hemophilus aphrophilus	Ampicillin, tetracycline, chloramphenicol, streptomycin
Hemophilus ducreyi	Tetracycline, sulfonamides, chloramphenicol, streptomycin
Hemophilus influenzae	Tetracycline, chloramphenicol, streptomycin, kanamycin, penicillin
Klebsiella pneumoniae	Gentamicin, kanamycin, polymyxin or colistin
Klebsiella rhinoscleromatis	Streptomycin, tetracycline, chloramphenicol
Moraxella liquefaciens	Penicillin, ampicillin, chloramphenicol, tetracycline
Moraxella duplex, var. nonliquefaciens	Penicillin, tetracycline, kanamycin
Pasteurella multocida (septica)	*Penicillin,* tetracycline, chloramphenicol
Pasteurella pestis	Streptomycin plus either tetracycline or chloramphenicol
Pasteurella pseudotuberculosis	Tetracycline, ? chloramphenicol, ? streptomycin
Pasteurella (Franciscella) tularensis	Streptomycin plus either tetracycline or chloramphenicol
Proteus mirabilis	Kanamycin, ampicillin, cephalothin or cephaloridine, chloramphenicol, penicillin, gentamicin

(Gram-Negative Bacilli, Continued from Page 374)

Organism	Drug of Choice
Proteus morganii	Kanamycin, chloramphenicol, gentamicin
Proteus rettgeri	Kanamycin, gentamicin
Proteus vulgaris	Kanamycin, chloramphenicol, gentamicin
Providence	Kanamycin, chloramphenicol, tetracycline, polymyxin or colistin
Pseudomonas aeruginosa	Gentamicin, polymyxin or colistin, oxytetracycline, chloramphenicol
Pseudomonas maltophilia	Polymyxin or colistin, chloramphenicol, kanamycin
Pseudomonas pseudomallei	Chloramphenicol, kanamycin, sulfadiazine, tetracycline
Pseudomonas stutzeri	Ampicillin, cephalothin, kanamycin, polymyxin or colistin
Salmonella typhi	Chloramphenicol, ampicillin
Salmonella, other than S. typhi	Chloramphenicol, ampicillin, cephalothin
Serratia marcescens	Gentamicin, kanamycin, chloramphenicol
Shigella	Ampicillin, cephalothin, kanamycin, tetracycline, chloramphenicol
Sphaerophorus necrophorus (Bacteroides funduliformis)	Tetracycline, chloramphenicol, penicillin, lincomycin
Streptobacillus moniliformis	Penicillin
Vibrio cholerae	Tetracycline, chloramphenicol
Vibrio fetus	Tetracycline, chloramphenicol, ampicillin, streptomycin

GRAM-NEGATIVE COCCI

Organism	Drug of Choice
Gonococcus (Neisseria gonorrhoeae)	Penicillin, tetracycline, erythromycin
Meningococcus (Neisseria meningitidis)	Penicillin, ampicillin, chloramphenicol, erythromycin, tetracycline, sulfadiazine

GRAM-POSITIVE BACILLI

Organism	Drug of Choice
Actinomyces israelii	*Penicillin*, tetracycline, chloramphenicol, cephalothin
Bacillus anthracis	*Penicillin,* erythromycin, tetracycline
Clostridium	*Penicillin,* tetracycline, chloramphenicol
Corynebacterium acnes	Tetracycline, ? lincomycin
Corynebacterium diphtheriae	Penicillin, erythromycin, cephalothin
Corynebacterium, other	Vancomycin, penicillin, erythromycin
Erysipelothrix rhusiopathiae	Penicillin, ? tetracycline
Listeria monocytogenes	Tetracycline, ampicillin, penicillin, erythromycin
Nocardia	Sulfonamides, cycloserine

GRAM-POSITIVE COCCI

Organism	Drug of Choice
Pneumococcus (Diplococcus pneumoniae)	Penicillin, erythromycin
Staphylococcus	Methicillin, cloxacillin or dicloxacillin, cephalothin or cephaloridine, nafcillin, vancomycin, lincomycin
Streptococci	
Anerobic and microaerophilic strep. (and cocci)	*Penicillin,* lincomycin, erythromycin, chloramphenicol, vancomycin
Enterococci	*Penicillin plus streptomycin,* chloramphenicol, vancomycin, penicillin plus kanamycin, ampicillin, (tetracycline for S. liquefaciens)
Group A beta-hemolytic strep.	*Penicillin,* erythromycin, ampicillin, cephalothin
Viridans group	*Penicillin,* vancomycin, cephalothin

SPIROCHETES

Organism	Drug of Choice
Borrelia recurrentis	Tetracycline, chloramphenicol, penicillin
Spirillum minus	*Penicillin,* erythromycin
Treponema pallidum	*Penicillin,* erythromycin, tetracycline

RICKETTSIAE, MYCOPLASMA, CHLAMYDIA (BEDSONIA)

Organism	Drug of Choice
Rickettsia	Tetracycline, chloramphenicol
Mycoplasma pneumoniae	Tetracycline, erythromycin
Psittacosis (ornithosis)	Tetracycline, chloramphenicol
Lymphogranuloma venereum	Tetracycline, chloramphenicol, sulfonamides

INVESTIGATIONAL ANTIMICROBIAL AGENTS

Alvin Davis, M.D.

The antimicrobial agents described below have not been approved for general use by the Food and Drug Administration as of the time of this publication. With one exception (saramycetin), they have been available to investigators in significant quantities for purpose of evaluation so that considerable data are usually available. However, the information presented may not prove to be entirely accurate as additional experience is acquired and reported.

Carbenicillin

Carbenicillin is the disodium salt of carboxybenzyl penicillin, a semi-synthetic penicillin. It is a bactericidal drug which is excreted rapidly unchanged into the urine.

Antimicrobial Activity—Carbenicillin is active against Gram positive organisms such as staphylococci, streptococci, and pneumococci, but its uniqueness is referable to its activity against Gram negative organisms not ordinarily susceptible to any other penicillin. It is active against some strains of *Pseudomonas aeruginosa, Proteus morgani, Proteus rettgeri* and *Proteus vulgaris.* It is also active against *Hemophilus influenza,* and about as active as ampicillin against *Escherichia coli, Proteus mirabilis,* and *Shigella* species. It is inactivated by staphylococcal beta lactamase. Because of the variability of susceptibility to this drug of the resistant Gram negative organisms, in vitro susceptibility tests are important in the rational use of this drug.

Dosage and Administration—Carbenicillin is suitable for intravenous or intramuscular administration. There is no oral preparation. Dosage depends upon severity of the infection and the susceptibility of the etiologic agent to the drug. Minimum dose is usually 1 gram every six hours, but doses or 30 grams per day of carbenicillin in addition to probenecid may be administered in severe or resistant infection. Carbenicillin may be administered intrathecally or intraventricularly in doses of 40 mg daily to patients with meningitis. High doses need not be used in urinary infection because approximately 70% of the drug appears in the urine within five hours after intramuscular administration.

Toxicity and Side Effects—Patients known to be allergic to any penicillin may manifest an allergic response to this drug. There are no known toxic effects produced by the drug.

Cephaloglycin

Cephaloglycin is a phenyl glycine analog of the antibiotic cephalothin suitable for oral use. It is a zwitterion and therefore contains no cation. It is bactericidal in its activity.

Antimicrobial Activity—In general, it is as active against Gram negative organisms as are cephalothin and cephaloridine. It is less active than cephaloridine against staphylococci. Because of in vitro instability of cephaloglycin, in vitro testing may be misleading unless it is recognized that both tube dilution and disc susceptibility tests may be in error because of inactivation of the drug and the subsequent growth of susceptible organisms. In addition, because of low serum levels achieved, susceptibility to low concentrations of the drug would have to be assured for treatment of infections other than those of the urinary tract.

Dosage and Administration—Tentative dosage range is 250 mg to 1 gram by mouth four times daily, preferably on an empty stomach. Peak serum levels two hours after a single 500 mg dose taken in the fasting state were between 2 and 3 mcg/ml. Urine concentrations after the same dose were usually greater than 300 mcg/ml.

Toxicity and Side Effects—The possibility of renal toxicity is suggested by animal toxicity studies which used large parenteral or intraperitoneal doses. This has not been observed in animals or humans to whom the drug has been administered by mouth. Allergic reactions may be expected in patients allergic to other cephalosporin C derivatives, and perhaps in patients allergic to penicillin as well.

Cephalexin

Cephalexin is a desacetoxy analog of the antibiotic cephaloglycin. It is a zwitterion and is bactericidal against susceptible strains. Its chief advantage is better absorption on oral administration, with resulting high serum levels.

Antimicrobial Activity—It is active against both Gram-negative and Gram-positive organisms susceptible to other cephalosporin derivatives. Although it appears to be less active on a weight basis against certain organisms than other cephalosporin derivatives, this effect is offset by the high serum levels achievable with therapeutic doses. There is evidence that some strains of *S. aureus* may develop resistance to the drug. There is not yet sufficient data to assess the extent or importance of this phenomenon.

Dosage and Administration—Tentative adult dosage is 250 to 500 mg three to four times daily. Food in the stomach interferes with absorption. A single 500 mg dose taken in the fasting state produced an average peak serum level of 18 mcg/ml in 12 adults. Approximately 70-80% of the drug is excreted unchanged into the urine within four hours of oral administration on an empty stomach.

Toxicity and Side Effects—There is little data on toxicity, but it appears that increased frequency of bowel movements or diarrhea may occur. There is no information concerning possible nephrotoxicity in clinical usage. Allergy to other cephalosporin derivatives, and perhaps to penicillin as well, may make allergic response to cephalexin likely.

Rifampicin (Rifampin)

Rifampicin (rifampin) is the amino methyl piperazine derivative of rifamycin S.V. The naturally occurring rifamycins from which this drug is derived were first isolated from cultures of *Streptomyces mediterranei* in 1959. It is unrelated chemically to other commonly available antibiotics. The mechanism of action is not fully understood but there is no evidence that it interferes with the synthesis of either cell wall, protein or nucleic acid. Unlike the parent rifamycin S.V., rifampicin is effective orally.

Antimicrobial Activity—The minimum inhibitory concentrations (MIC) for most strains of *Staphylococcus aureus, Streptococcus pyogenes,* and *Diplococcus pneumoniae* are very low (<0.5 mcg/ml). The MIC for Gram-negative pathogens and for enterococcus is higher but many strains are inhibited by 10 mcg/ml or less. The manufacturer is presently restricting investigational use to therapy of mycobacterial and gonococcal infections. All strains of *M. tuberculosis var. hominis* examined were inhibited by levels of 1 mcg/ml or less. Atypical mycobacteria are also often susceptible.

The significance of a potential problem of early development of resistance on the part of some microorganisms remains to be determined.

Dosage and Administration — Rifampicin is available for oral use only. The usual adult dose is 300 mg tid, preferably on an empty stomach. A peak level of 3 to 5 mcg/ml is reached two to three hours after a single 300 mg dose and the level at 12 hours is not measurable. The drug is excreted primarily into the bile, but ten percent to 15 percent is recovered in the urine.

Toxicity and Side Effects — Granulocytopenia (apparently reversible) has been reported. Rarely, mild headache and gastrointestinal complaints have been observed.

Saramycetin

Saramycetin is an anti-fungal drug which has been known previously by the code designations RO 2-7758 and X-5079C. It is a polypeptide produced by a species of *Streptomyces*. Technical difficulties have limited the availability of this drug markedly despite the length of time it has been known.

Antimicrobial Activity—This drug appears to have a clinically useful level of activity for the treatment of infections caused by *Blastomyces dermatitidis* and *Histoplasma capsulatum,* and to a lesser extent *Sporotrichum schenkii.* Activity against *Coccidioides immitis* is of questionable usefulness, and it is ineffective in *Cryptococcus neoformans* infections.

Dosage and Administration—Usual dose reported is 3 to 5 mg/kg/day subcutaneously for periods of four to six weeks.

Toxicity and Side Effects—Alteration in liver function tests was almost universal in patients treated. Results of liver function tests usually returned to normal in patients without pre-treatment abnormalities of liver function. Pre- and post-treatment liver biopsies have shown variable tissue changes. Other side effects of treatment that have been observed are eosinophilia, local pain and inflammation at injection site, febrile reactions and urticarial reactions.

ANTIBACTERIAL AGENTS IN RENAL INSUFFICIENCY

IRWIN ZIMENT, M.B., M.R.C.P.

1. Excretion of Antibacterial Agents:

Most antibiotics and chemotherapeutic agents, and their degradation products, are excreted mainly by the kidneys, thus necessitating reduc-

TABLE 1.—*Dosage Modifications Required in Renal Insufficiency.*
(Tabulation of the antibacterial agents on the basis of renal and extra-renal toxicity as determinants for dosage modification in renal insufficiency.)

MAJOR MODIFICATION			MINOR MODIFICATION	NO MODIFICATION	CONTRA-INDICATED
Major Renal Toxicity		*? Renal Toxicity*	*No Renal Toxicity*		
Major Extra-Renal Toxicity	*Minor or No Extra-Renal Toxicity*	*Major Extra-Renal Toxicity*	*Some Extra-Renal Toxicity*	*(Avoid High Dosage)*	
Kanamycin	Polymyxin	Streptomycin	Chloramphenicol	Penicillin‡	Nitrofurantoin
Gentamicin	Colistin	Tetracycline*	Lincomycin**	Ampicillin	Nalidixic acid
Neomycin†	Bacitracin†	Oxytetracycline*	Cephalothin**	Methicillin***	Methenamine
Vancomycin	Cephaloridine†	Chlortetracycline*	INH	Other penicillins	Long-acting sulfonamides
Amphotericin			PAS†	Erythromycin	Long-acting tetracyclines
(? Short-acting sulfonamides)			Cycloserine	Novobiocin	
			(? Ethambutol)		

*Intravenous tetracycline causes higher peak blood levels and such therapy is more hazardous than oral dosage. Particular caution should be observed in pregnant women. Out-dated tetracycline products should never be used, since rare cases of the Fanconi syndrome have resulted; this occurred particularly under moist storage circumstances in products containing citric acid in the formulation. Chlortetracycline is rarely used now.

**Cephalothin and lincomycin do not appear to be toxic in renal failure, but lower dosage is recommended since retention of the drugs occurs, making usual dosage regimens excessive.

***Methicillin has caused hypersensitivity nephrotoxic reactions. Large dose therapy can introduce an appreciable sodium load, which could be dangerous in renal failure.

†These agents should be avoided in uremic patients.

‡Large dose penicillin therapy in renal failure can introduce a dangerous electrolyte load, and also carries a marked risk of neurotoxicity.

tion of dosage in patients with renal insufficiency. This is important not only in the case of nephrotoxic drugs, but also for those drugs which have major extrarenal toxicity. Reduced dosage is also desirable for most non-toxic antibacterial agents which are cleared by the kidney, since normal dosage would produce accumulation in the body, whereas lower dosage regimens offer advantages in economy and ease of administration with less risk of superinfection.

The appropriate dosage to administer is based upon whether or not the drug is excreted by the kidney:

(1) *Cleared mainly by the kidney:*

(a) *Major nephrotoxic agents:* kanamycin, neomycin, gentamicin, polymyxin, colistimethate, vancomycin, cephaloridine, sulfonamides, amphotericin, bacitracin

(b) *Possibly nephrotoxic agents:* tetracycline, streptomycin

(c) *Non-nephrotoxic agents* (in usual dosage):

(i) No extra-renal toxicity: penicillin, methicillin, ampicillin, oxacillin, cloxacillin, dicloxacillin, nafcillin, cephalothin, lincomycin

(ii) Some extra-renal toxicity: INH, PAS

(2) *Not cleared by kidney* (in unchanged form):

(a) *Potentially toxic:* chlortetracycline, chloramphenicol

(b) *Non-toxic:* erythromycin, novobiocin

For dosage modifications see Tables 1 and 2.

2. Antibacterial Agents Contraindicated in Renal Failure:

a. *The antituberculosis drugs* — Pyrazinamide, ethionamide, cycloserine, viomycin and ethambutol are best avoided in patients with marked renal impairment. Only viomycin is nephrotoxic, but the others all have marked extrarenal toxicity. No dosage schedule for use of these second-line drugs in renal failure can be recommended as safe since information in this area is inadequate; only INH, streptomycin, PAS, and possibly ethambutol and cycloserine should be used. INH appears to be very safe in azotemia unless the patient is malnourished or alcoholic; in such cases reduced INH dosage with pyridoxine supplements is advisable. Many uremic patients have difficulty tolerating PAS, and unless its use is considered to be essential, it should be avoided in severe renal insufficiency. Streptomycin should be used with appropriate dosage reduction in uremia; elderly patients are particularly liable to suffer toxic effects, and should be carefully monitored.

b. *Agents used for urinary tract infections*—

(1) *Sulfonamides* should not be used in patients who cannot maintain adequate fluid intake or when renal insufficiency is present. The dangers of crystalluria and extra-renal toxicity make these drugs unsuitable, unless therapy can be carefully controlled.

(2) *Nitrofurantoin* and *nalidixic acid* are

TABLE 2.—*Antibiotic Dosage in Renal Failure*

Antibiotic	*Normal-36% Normal Renal Function (Normal Creatinine)*	*35%-10% Normal Renal Function (Creatinine 1.5-5.0)*	*9%-0% (Anuria) of Renal Function (Creatinine>5.0)*
Aq. Penicillin G	Normal dose depending on infection	Normal dose, but high dosage therapy contraindicated	
Ampicillin	Normal dose depending on infection	Normal dose	Normal dose
Oxacillin (IM or IV)	Normal dose depending on infection	Normal dose	0.25-1.0 Gm q 6 h
Cloxacillin (oral)	Normal dose depending on infection	Normal dose	0.25-0.5 Gm q 6 h
Dicloxacillin	Normal dose depending on infection	Normal dose	0.25-0.5 Gm q 6 h
Methicillin	1.0-3.0 Gm q 3-6 h	1.0-2.0 Gm q 3-6 h	1.0-2.0 Gm q 4-8 h
Nafcillin	0.25-3.0 Gm q 3-6 h	0.25-1.0 Gm q 3-6 h	0.25-1.0 Gm q 3-6 h
Cephalothin	1.0-3.0 Gm q 3-6 h	1.0-2.0 Gm q 6-8 h	1.0 Gm q 6-24 h
Cephaloridine	0.25-1.0 Gm q 6 h	Do not use	Do not use
Lincomycin (oral)	0.5 Gm q 6-8 h	0.25 Gm q 6-8 h	0.25 Gm q 8-12 h
Lincomycin (IM, IV)	0.6 Gm q 8-12 h	0.3 Gm q 8-12 h	0.2 Gm q 8-12 h
Erythromycin	0.25-0.5 Gm q 6 h	0.25-0.5 Gm q 6 h	0.25-0.5 Gm q 6 h
Novobiocin	0.25-0.5 Gm q 6 h	0.25-0.5 Gm q 6 h	0.25-0.5 Gm q 6 h
Tetracycline and	0.25-0.5 Gm q 6 h	1st day: 0.25 Gm q 6 h Then: 0.5 Gm q 1-2 days	1st day: 0.25 Gm q 6 h Then: 0.5 Gm q 3-4 days
Oxytetracycline (oral)		(do not give intravenously)	
Chlortetracycline (oral)	0.25-0.5 Gm q 6 h	0.25-0.5 Gm q 6 h	Use not advised
Chloramphenicol	0.25-1.0 Gm q 6 h	0.25-1.0 Gm q 6 h	(?) Normal dose
INH	300 mg q.d. (in 1 dose)	100 mg q 8 h + pyridoxine	(?) 100 mg qd + pyridoxine
PAS	4 Gm t.i.d.	2 Gm t.i.d.	Do not use
Neomycin (oral)	1.5 Gm q 4-6 h	Do not use	Do not use
Kanamycin (oral)	1.5 Gm q 4-6 h	1.0 Gm q8-12h	Do not use
Kanamycin (I.M.)	7.5 mg/kg/day q12h	1st day: 7.5 mg/kg q12h (x2) Then 7.5 mg/kg q1-2 days	1st day: 7.5 mg/kg (1 dose only) Then: 7.5 mg/kg q3-6 days
Streptomycin	0.5-1.0 Gm q12h	1st day: 0.5 Gm q12h (x2) Then 0.5 Gm q1-2 days	1st day: 0.5 Gm q12h (x2) Then: 0.5 Gm q3-4 days
Vancomycin	1 Gm q12h	0.5 Gm q2-3 days	1.0 Gm q10 days
Polymyxin (I.M., I.V.)	0.8 mg/kg q8h	1st day: normal dosage Then: 0.8 mg/kg q48h	1st day: normal dosage Then: 0.8 mg/kg q3d
Colistimethrate (I.M.)	1.6 mg/kg q8h	1st day: normal dosage Then: 1.6 mg/kg q36-38h	1st day: normal dosage Then: 1.6 mg/kg q3d
Gentamicin (I.M.)	0.3-1.5 mg/kg q8h-q12h	1st day: normal dosage Then: 0.3-1.0 mg/kg q12-24h	1st day: normal dosage Then: 0.3-1.0 mg/kg q3-4 days
Nitrofurantoin (oral)	100 mg q6h	Do not use	Do not use
Nitrofurantoin (I.V.)	180 mg q12h	Do not use	Do not use
Nalidixic acid	0.5-1.0 Gm q6h	Do not use	Do not use
Sulfonamides	Normal dose	Do not use	Do not use
Methenamine	1.0 Gm q6h (+ urine acidification to pH 5.0-5.5)	Do not use	Do not use
Amphotericin	1.0 mg/kg 3 x/week	1.0 mg/kg 2 x/week	Unknown
	(Dosage depends on effect on creatinine clearance)		

specifically indicated for the treatment of urinary tract infections, but are only effective when renal function is normal, and should not be used otherwise since extra-renal toxicity may result.

(3) *Methenamine* is only effective in the treatment of urinary tract infections when the urine pH is reduced to 5-5.5 (e.g. by giving methionine). Acidification of the urine in renal failure may prove impossible, and systemic acidosis can result from giving acidifying drugs. Therefore, methenamine, although relatively non-toxic, is unsuitable for patients with renal insufficiency.

3. Principle in the Treatment of Infections in the Presence of Renal Insufficiency:

(1) The least nephrotoxic agent should always be selected, (preferably on the basis of bacteriologic susceptibility studies).

(2) A relatively non-toxic (all types of toxicity

considered) antibiotic should be given if suitable; e.g., penicillin G, ampicillin, penicillinase-resistant penicillins, erythromycin, cephalothin.

(3) A toxic agent should be given for as short a period as is consistent with effective eradication of the infection.

(4) Frequent serum creatinine levels and creatinine clearance, if possible, should be obtained to guide changes in drug dosage. Urine output should be watched.

(5) The patient's clinical response is as important a guide to dosage as are the recommendations in Table 2.

(6) Avoid long-acting preparations of penicillins, tetracyclines, sulfonamides or other drugs.

(7) *Chlortetracycline* is more readily inactivated than other tetracyclines. However, it may have a catabolic effect and therefore its use in the presence of azotemia is no longer advised.

(8) *Chloramphenicol* degradation products could accumulate in patients with renal insufficiency; it is still not clear whether or not these metabolites are toxic.

(9) *Sulfonamides* may present an added risk to the patient with renal insufficiency, although one study suggests that sulfadimidine is not retained and is effective therapy for urinary infections in the presence of azotemia.

(10) *Amphotericin* therapy induces renal defects in most recipients; while these are initially reversible, long-term intravenous administration often causes permanent damage, and a loss in renal function may have to be accepted if the fungal infection is to be effectively treated. The modification of dosage which may be necessary in patients with renal insufficiency is unknown.

4. Nephrotoxic Antibiotics in Renal Failure:

Severe infections in patients with renal failure may necessitate therapy with nephrotoxic agents, and the risk of further deterioration in renal function must be balanced against the dangers of the infection. Renal function may actually be improved if the infection is in the kidneys or if there is prerenal failure associated with systemic infection.

If the patient has end-stage renal disease, the further damage that may occur while using a nephrotoxic agent is relatively unimportant if the patient can subsequently be admitted to a chronic dialysis program. This applies in particular to the use of polymyxin or colistimethate whose extrarenal toxicity is not a major problem; however, high blood levels of these drugs may produce apnea (the other neurotoxic effects of the polymyxins are always reversible). Cephaloridine and bacitracin (which is rarely used) are likewise nephrotoxic, but differ from the polymyxins in having no extra-renal toxicity, and theoretically may be safely used in irreversible renal failure, whereas they should not be used if there is hope of renal improvement.

5. Treatment of Urinary Tract Infections:

This usually proves to be unsatisfactory in patients with chronic renal failure since the concentration of antibiotics in the urine, and possibly in the renal parenchyma, is generally inadequate. Treatment with the largest recommended dosage of the less toxic antibiotics should be tried, with repeated urine culture as a guide to the success of therapy.

It is of interest that the combination of penicillin or ampicillin with a penicillinase-resistant penicillin may occasionally give a synergistic bactericidal effect against a wide spectrum of bacteria including *Pseudomonas.* A return of infection is usual after antibacterial therapy is terminated, however.

It is important to remember that the effectiveness of many antibacterial agents may be very dependent upon the pH of the medium:

(1) *More effective in alkaline urine:* erythromycin, streptomycin, kanamycin, gentamicin, sulfonamides.

(2) *More effective in acid urine:* tetracyclines, novobiocin, cycloserine, nitrofurantoin, methenamine compounds.

(3) *Relatively independent of pH:* chloramphenicol, ampicillin, (?) polymyxins.

In the presence of renal insufficiency, attempts to alter the urinary pH may not be possible without serious changes in acid-base balance.

6. Evaluation of Renal Function:

The serum creatinine provides a good guide to renal status, and serial endogenous creatinine clearances provide the best guide to changes in renal function when using a nephrotoxic antibiotic. Even a barely elevated serum creatinine is consistent with a 75 percent loss of renal function. Restriction in dosage of drugs cleared by the kidney is required only when renal function is less than 35 percent normal. An initial creatinine determination should always be obtained prior to starting therapy with a nephrotoxic antibiotic and frequent creatinine determinations should be obtained during therapy, even in patients with no known renal disease. Urine examination is not so helpful, since an abnormal sediment may appear during therapy without any significant damage to the kidney having occurred.

7. Extra-renal Toxicity of Antibacterial Agents:

The non-renal toxic effects of kanamycin, vancomycin, streptomycin, tetracyclines (especially intravenous), and possibly chloramphenicol and INH are an increased hazard when renal function is borderline. Monitoring of serum creatinine safeguards against inadvertent accumulation of these drugs when renal function is suspect. Kanamycin is a particular danger since rapid onset of hearing loss has followed in some patients with over-dosage; single dose therapy with this drug should not exceed 7.5 mg/kg since deafness has been recorded after a single dose of 1 Gm in a patient with renal impairment.

8. Antibiotic Serum Assays:

These are rarely performed by routine hospital laboratories, but should be helpful in patients with renal failure who are receiving potentially toxic agents. This applies both to nephrotoxic agents and to those with major toxicity in other areas.

It is unfortunate that such exact guidance can rarely be employed, since reliable and meaningful results can only be obtained from laboratories which do assays regularly. Further, assays take time, and the delayed results may not help in a critical case.

The therapeutic range for an antibiotic depends upon the particular infection and the toxic level is not always known. The following levels should prove therapeutically adequate, and should not be exceeded if toxic effects are to be avoided. (Blood samples should be taken about two hours after administering the drug):

Streptomycin 20-40 mcg/ml
Chloramphenicol 15-30 mcg/ml
Kanamycin 10-20 mcg/ml
Vancomycin 10-20 mcg/ml
Colistin 10-20 mcg/ml
Gentamicin 7-10 mcg/ml
Polymyxin 5-10 mcg/ml
Tetracycline 3-10 mcg/ml
INH 1-3 mcg/ml

It may also be useful to check the levels at periods of 24 hours after drug doses for a guide to possible adjustment in frequency of administration. When treating a urinary tract infection in renal insufficiency it may be useful to assay the urine to ensure that adequate amounts of the agent do get excreted. If insufficient amounts are excreted, then administering the agent may prove futile and introduces an unnecessary hazard. Assays of antibiotics in urine are simpler to perform than are serum assays.

9. Recovery Phase Following Acute Renal Failure:

The diuretic phase following acute renal shutdown is associated with persistence of the impairment of excretory function. Normal dosage of those antibiotics excreted principally by the kidney remains hazardous until the creatinine clearance has returned to normal. For practical purposes a creatinine clearance of less than 10 ml/min implies anuria.

10. Hepatorenal Failure:

The association of hepatic failure with renal insufficiency necessitates further reduction in dosage of certain of those antibiotics excreted or inactivated by the liver, i.e. ampicillin, tetracycline group, chloramphenicol, erythromycin (estolate), novobiocin, lincomycin and possibly cephalothin. In managing hepatorenal failure oral kanamycin is safer than neomycin, but either may accumulate to reach toxic levels in the blood. For further details see section on Antibiotics and Liver Disease.

11. Use of Antibacterial Agents in Patients on Dialysis:

Adjustments in antibiotic dosage may be required for anuric patients sustained on peritoneal dialysis or hemodialysis. Information is incomplete for many antibiotics, and *the following schedule is only an approximate guide.* Drugs not mentioned below should not be used since information on them is not available, and safer antibiotics can be used.

a. *Dosage as in anuria* (see Table 2):

(1) *Excreted or inactivated by non-renal mechanisms:*

erythromycin
chloramphenicol
(?ampicillin*)

(2) *Not removed by dialysis:*

polymyxin
colistin
vancomycin
lincomycin
oxacillin
cloxacillin
methicillin

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*Information inadequate.

(?penicillin*)
(?dicloxacillin*)

b. *Minor dosage adjustment required* — for drugs which are partially removed by dialysis:

(1) *Hemodialysis*—dosage schedules are relatively well established for patients on chronic twice-weekly dialysis:

tetracycline
(oral) — 0.5 Gm post-dialysis
streptomycin — 0.5 Gm post-dialysis
gentamicin — 1 mg/kg post-dialysis
kanamycin — 7.5 mg/kg post-dialysis
INH — 300 mg post-dialysis then 100 mg + pyridoxine q 24 h

(2) *Peritoneal dialysis* — Since long-term regular peritoneal dialysis is rarely used, guidelines for antibiotic dosage are less clearly established. Insufficient amounts of tetracycline are removed to be of significance, and the dosage recommended for the anuric patient should be used. More substantial amounts of kanamycin and streptomycin (and possibly gentamicin) are removed; the dosage suggested for patients on hemodialysis could be used, but the appropriateness of this is uncertain.

c. *Dosage adjustment probably required*—information not adequate:

amphotericin
cephalothin
cephaloridine

It should also be noted that dialysis (peritoneal or hemodialysis) should be used in the management of overdosage with kanamycin and possibly streptomycin and gentamicin, but is unlikely to be of value with other nephrotoxic antibiotic intoxications.

Antibiotics should not be added to the dialysing fluid used in peritoneal dialysis, since they are of no value as prophylaxis against infection and may get absorbed and accumulate in the body.

Table 2 provides an approximate guide to dosage for antibacterial agents in patients with renal insufficiency. Much of the information currently available is inadequate, and *this guide cannot be regarded as definitive.* It should be appreciated that in any individual patient such a dosage guide could result in inadequate or hazardous drug levels unless clinical and laboratory guides are obtained concurrently and appropriate dosage adjustments made as necessary.

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*Information inadequate.

ANTIBIOTICS AND LIVER DISEASE

Irvin Jacobs, M.D.

The following outline is an attempted compilation of known information to serve as a guide in using antibiotic therapy in patients with (a) underlying liver disease and (b) acute liver and gallbladder infections. Unfortunately, precise information is inadequate for many of the drugs. For some drugs very little human data is available for liver tissue antibiotic concentrations, liver histology during treatment, bile levels, and precise metabolic processes in the liver. Indeed, for many older drugs and drugs that are little used, even animal data is scanty.

It is emphasized that often animal data is not applicable to man. A good example is isoniazid, which given long term to dogs produces fatty changes and jaundice; this development is rare in man.

For the most part in treating patients with preexisting liver disease who develop infections outside the liver, one should use caution in prescribing drugs known to be dependent on liver for inactivation or excretion. Usually a safer substitute drug can be found. If a potentially toxic drug must be used, blood levels can be useful in monitoring the dose to within safe limits. One should also take care to avoid use of hepatotoxic non-antibiotic drugs concomitantly.

On the other hand, drugs metabolized and/or excreted by the liver are theoretically ideal for treatment of acute infections of liver and biliary tract.

I. Penicillin G

1. Metabolism by liver: Only minor fraction is ordinarily handled by liver, but in impaired renal function the liver may be a major excretion route via bile.

2. Liver tissue levels: Significant

3. Bile levels: Significant concentration

4. Liver toxicity: Rarely, as part of a generalized hypersensitivity reaction

5. Dose in liver disease:

(a) No change if renal function is good

(b) Reduce dose in circumstance of combined kidney and liver disease.

6. Comment: All penicillins are concentrated in bile even if absolute amount of hepatic excretion is small.

II. Alpha-phenoxy-penicillins

A. Phenoxymethyl

B. Phenoxyethyl (phenethicillin)

C. Phenoxybenzyl (phenbenicillin)

Generally the information for penicillin G applies also for this group. One unique feature of phenbenicillin is that 20% of a dose appears in urine in the form of two metabolities, rather than in unchanged form as with the other penicillins. Site of the metabolic conversion is unknown.

III. Beta Lactamase-Resistant Penicillins

A. Methicillin. Generally the information for penicillin G applies to methicillin.

B. Oxacillin

C. Cloxacillin

D. Nafcillin

Oxacillin and nafcillin have a high percentage excretion into bile. Indeed, with nafcillin, up to 90% of an I.V. dose is accounted for in bile. Oxacillin has induced mild reversible SGOT rises, in one case with a palpable liver.

IV. Broad-Spectrum Penicillins

A. Ampicillin

B. Hetacillin

C. Carbenicillin

Generally the information for penicillin G applies to this group. Ampicillin concentrations in bile may reach as high as 300 times that concurrently present in the plasma; however, the kidneys still account for the major function of the excretion, perhaps 80 percent or more.

In two reports, up to 30 percent of patients on hetacillin 1-2 Gm/day P.O. or I.M. developed laboratory liver function abnormalities without clinical signs; these usually reverted after stopping drug.

I.M. injection of ampicillin in doses of 1 Gm or more can be associated with modest SGOT elevations, which return to normal after stopping drug. The SGOT is possibly released from muscle, rather than liver.

V. Cephalosporins

A. Cephalothin

1. Metabolism by liver: 70-80% usually excreted unchanged in urine. However, it can be inactivated by deacetylation (presumably in liver), then excreted in urine.

2. Liver tissue levels: No information on humans; not concentrated in rats' livers.

3. Bile levels: No good data available.

4. Liver toxicity: Occasional SGOT rise

5. Dose in liver disease: Advisable to decrease in presence of combined renal-hepatic disease.

6. Comment: Many patients develop a positive Coombs' test on drug, but this doesn't correlate with a hemolytic state.

B. Cephaloridine

1. Metabolism by liver: No data; but 70-75% of the drug is accounted for in unchanged form in urine. (There is no acetyl group to split off this compound, as there is with cephalothin.)

2. Liver tissue levels: In rabbits on 200 mg/kg simultaneous levels are:

	LIVER (mcg)	*SERUM (mcg)*
@ ½ hr.	30	100
@ 4 hr.	25	10

In a patient on 1 Gm q4h who died, assay of serum and liver tissue respectively were 58 mcg/ml and 31 mcg/ml.

3. Bile levels: Equal to or below serum.

4. Liver toxicity: Drug may regularly cause modest rise in SGOT, which often reverts while drug is continued. May regularly cause prolonged prothrombin time (up to 29 sec.), though no hemorrhage reported.

5. Dose in liver disease: Same as for cephalothin.

VI. Streptomycin and Dihydrostreptomycin

1. Metabolism by liver: Small fraction is secreted into bile.

2. Liver tissue levels: Appreciable.

3. Bile levels: Not concentrated; up to 10-20 mcg/ml on high doses.

4. Liver toxicity: Rarely reported; also rarely may aggravate existing liver disease.

5. Dose in liver disease: No change.

VII. Tetracyclines

Chlortetracycline, oxytetracycline, tetracycline, demethylchlortetracycline, methacycline, doxycycline

1. Metabolism by liver: All tetracyclines are concentrated in liver and excreted via bile into intestine, where they are reabsorbed. Variable amounts of each member of this drug family are

thereafter eliminated in urine. Chlortetracycline has only 18% eventually eliminated by urine, whereas tetracycline has 60%, oxytetracycline 70%, and methacycline and demethylchlortetracycline 60-70% eliminated eventually in urine. Methacycline and demethylchlortetracycline have prolonged half-lives in the serum because of slower (½) renal clearance than that of tetracycline or oxytetracycline.

2. Liver tissue levels: All are concentrated.

3. Bile levels: 5-32 x the serum level.

4. Liver toxicity: With excess parenteral dose, patients get abnormal LFT's progressing to acidosis, shock, coma and death. Liver lesion is fatty vacuolization with little or no necrosis or biliary stasis. Other organs which may suffer simultaneous toxicity are pancreas, kidneys and brain. Pregnancy and chronic renal disease seem to predispose patients to this type of hepatotoxicity.

5. Dose in liver diseases: Some studies show ½-⅔ of patients with pre-existing hepatic disease get increased fat in liver cells while on tetracyclines. This may revert after stopping drug.

Recommend 1 Gm/day as maximum parenteral dose or use different drug in pregnancy, advanced liver disease, renal disease, or combined hepatic-renal disease. Avoid chlortetracycline completely in liver disease. If dosage adjustment is necessary, avoid exceeding a blood level of 10 mcg/ml.

6. Comments:

(a) By fluorescence and autoradiography, it is demonstrated that liver and kidney concentrate tetracyclines (in mitochondria) more than other organs. Tetracyclines have adverse effects on several hepatic enzymes.

(b) Inactivated chlortetracycline causes same toxic hepatic changes as the active drug; so hepatic toxicity appears not related to antibacterial activity (in mice, dogs).

(c) Tetracyclines may reduce blood coagulation by altering physicochemical characteristics of blood lipoproteins.

(d) Via probable changes in intestinal flora, tetracyclines may decrease plasma prothrombin, and increase urine bilirubin while decreasing urine urobilinogen. This ordinarily causes no clinical problem.

VIII. Chloramphenicol

1. Metabolism by liver: 85-95% is conjugated in liver to monoglucuronide; 3% is further converted to aryl amines and aryl nitro derivatives. Most of above is secreted then by kidney tubules.

2. Liver tissue levels: Concentrated.

3. Bile levels: Average ½ that of plasma.

4. Liver toxicity: Rare.

5. Dose in liver disease: Use caution. If ascites or jaundice is present, use under 25 mg/kg/day or another drug.

6. Comments:

(a) Bone marrow toxicity correlates with high serum levels of free drug; there is no known correlation with levels of metabolic products. It is desirable to keep serum level below 25 mcg/ml of free drug. Though overall chloramphenicol metabolism isn't greatly reduced in hepatic insufficiency, conjugation is slowed and allows more vulnerability to bone marrow toxicity.

(b) Newborns are vulnerable to "grey syndrome" due to immature hepatic and renal function.

IX. Macrolides

A. Erythromycin

1. Metabolism by liver: Major excretory pathway; it is excreted into bile in active form.

2. Liver tissue levels: Concentrated.

3. Bile levels: Concentrated to 5x plasma levels. The estolate form is excreted less in bile than other forms.

4. Liver toxicity: Only by estolate form. Up to 16% of patients after 10-14 days' therapy or repeated courses get elevated transaminase; up to 4% get jaundice with hepatitis symptoms and cholestatic hepatitis on biopsy.

5. Dose in liver disease: Avoid estolate form. Other forms in usual dosage.

6. Comments: Estolate-induced hepatitis is a hypersensitivity reaction. Look for eosinophilia. The syndrome may be reactivated later with a small single oral re-challenge dose of drug.

B. Oleandomycin and triacetyloleandomycin

1. Metabolism by liver: Major.

2. Liver tissue levels: No good data available.

3. Bile levels: Up to 10-15x the peak serum level.

4. Liver toxicity: None from oleandomycin. On triacetyloleandomycin 1 Gm qd x 14 days, up to over 50% of patients may get abnormal liver function tests with or without clinical symptoms. Changes may be dose dependent. Liver biopsies show mixed changes with hepatocellular damage, cholestasis, periportal infiltration and eosinophilia.

5. Dose in liver disease: Avoid.

X. Lincomycin

1. Metabolism by liver: Major; it is excreted and re-excreted via enterohepatic circulation.

2. Liver tissue levels: No data.

3. Bile level: High; can be 10-20x the serum level.

4. Liver toxicity: Occasional jaundice and/or abnormal liver function tests which clear rapidly, sometimes even while drug is continued. No histological information available.

5. Dose in liver disease: Half-life of drug is doubled. Accordingly drug dose should be reduced, or drug avoided entirely.

6. Comment: Relatively new drug, and experience incomplete.

XI. Novobiocin

1. Metabolism by liver: Major.

2. Liver tissue levels: No good data available.

3. Bile levels: 1½-8x serum level.

4. Liver toxicity: uncommonly, liver cell necrosis; occasional patients get biochemical lesion.

5. Dose in liver disease: Unknown, but probably is best to avoid.

6. Comments: This drug may induce "jaundice" by five different methods, all generally uncommon:

(a) Inhibition of glucuronyl transferase in newborns. Up to 7% get high indirect bilirubin and danger of kernicterus without associated liver cell morphological damage.

(b) After 2-14 days' therapy, 0.6% of patients get yellow discoloration of plasma, skin, and sclerae; this is controversially held to be secondary to a circulating lipochrome pigment degradation product of novobiocin.

(c) Occasional adults get increased unconjugated bilirubin and BSP retention with no evidence of morphological disease.

(d) Occasional hemolytic anemia.

(e) Occasional hepatocellular morphological damage with or without cholestasis.

XII. Kanamycin-Neomycin-Paromomycin Group

A. Kanamycin

1. Metabolism by liver: Nil.

2. Liver tissue levels: No data.

3. Bile levels: Up to 10-20x serum levels (but absolute amount is less than 0.5% of total amount of a 1 Gm test dose).

4. Liver toxicity: No.

5. Dose in liver disease:

(a) No change in parenteral dose.

(b) For oral form, see comments.

6. Comments:

In severe liver disease, oral kanamycin at 8 Gm/day eventually builds serum levels to therapeutic range. This effect is even greater with hepatic disease and azotemia. Accordingly, such patients on gut sterilization with kanamycin should be watched for deafness and increasing nephropathy.

B. Neomycin

1. Metabolism by liver: No.

2. Liver tissue levels: No data.

3. Bile levels: No good data available.

4. Liver toxicity: No.

5. Dose in liver disease: No more than 6 Gm P.O. for gut sterilization. If azotemia also present, kanamycin is preferred.

6. Comments: Same apply as for kanamycin. Notably with hepatic disease and azotemia, blood levels on 4 Gm/day P.O. may eventually reach those achieved on parenteral therapy in normals.

C. Paromomycin

This drug is only used orally for gut sterilization, and is only minimally absorbed. There is no liver toxicity. Probably kanamycin is preferred for gut sterilization in hepatic coma with azotemia.

XIII. Polymyxin - Colistin Group

1. Metabolism by liver: Minor, if any.

2. Liver tissue levels: No good data available.

3. Bile levels: Low.

4. Liver toxicity: No.

5. Dose in liver disease: No change.

XIV. Vancomycin

This drug is minimally, if at all, metabolized by liver. Very little is present in bile. No liver toxicity is reported.

XV. Nitrofurantoin

1. Metabolism by liver: 50-60% is metabolized at unknown site.

2. Liver tissue levels: No good data available.

3. Bile levels: No good data available.

4. Liver toxicity: Rarely, causes a hypersensitivity hepatitis with cholestasis, focal necrosis, infiltrates, eosinophils.

5. Dose in liver disease: Probably no change.

6. Comment: May cause hemolytic anemia with jaundice in G6PD deficient patients.

XVI. Sulfonamides

1. Metabolism by liver: Metabolism is significantly, but not solely by liver (acetylation, glucuronidation, and/or oxidation), then excreted into urine.

2. Liver tissue levels: Significant.

3. Bile levels: Similar to plasma.

4. Liver toxicity: Two types, not influenced by dose: direct hepatotoxicity and hypersensitivity. Either may go on to acute yellow atrophy.

5. Dose in liver disease: Best to avoid sulfas.

(a) Pre-existing nutritional liver disease may predispose to sulfonamide hepatotoxicity.

(b) Kidneys appear to be more susceptible to damage by sulfas in patients with chronic liver disease.

(c) Neonates have reduced acetylation, thus require less dose for therapeutic blood levels.

6. Comments:

(a) Incidence of reported hepatic injury secondary to sulfonamides is greatly decreased (to 0.1%) since the introduction of sulfadiazine and subsequent other new compounds.

(b) Acetylated and glucuronide forms circulating in blood prior to renal excretion contribute to toxicity but not to antibacterial effect.

(c) Sulfas may induce hemolytic anemias in G6PD deficient patients.

(d) Long-acting forms are particularly dangerous in the event of a toxic reaction since drug levels persist long after the drug is discontinued.

XVII. Amphotericin B

1. Metabolism by liver: Minor.

2. Liver tissue levels: No good data available.

3. Bile levels: No good data available.

4. Liver toxicity: May be rarely idiosyncratic, or due to excess dose (i.e., greater than 1 mg/kg/dose). The picture is acute failure with toxic degeneration, fatty liver and cholestasis.

5. Dose in liver disease: Unknown, but caution advised.

XVIII. Antituberculosis Drugs

A. Streptomycin: See above.

B. Isoniazid.

1. Metabolism by liver: 40-90% is excreted by kidneys; but a significant variable amount is inactivated by acetylation and other changes via liver enzyme(s), then excreted in urine.

2. Liver tissue levels: High.

3. Bile levels: Data in rabbits suggest 1½x the average serum level.

4. Liver toxicity: Rarely on therapeutic doses, patients may get either toxic or hypersensitivity hepatitis.

5. Dose in liver disease: Probably no change.

6. Comments: About 50% of patients are "slow inactivators," an autosomal homozygous recessive trait, i.e., they acetylate INH slowly, thereby having prolonged active drug levels. Slow inactivators should take pyridoxine daily.

Some workers feel "rapid inactivators" should get maximum doses for T.B. meningitis, but standard doses for pulmonary T.B. are adequate.

Note: Pyridoxine is a coenzyme of transaminases, and given daily may cause spuriously elevated transaminase activity.

C. Para-aminosalicylic acid

1. Metabolism by liver: 50-65% is acetylated (possibly by a liver enzyme), then excreted into urine.

2. Liver tissue levels: High.

3. Bile levels: No good data available.

4. Liver toxicity:

(a) Generalized hypersensitivity reactions (2-5%) may progress to include liver cell necrosis (uncommon), and/or cholestasis; it may be fatal.

(b) May suppress prothrombin formation in liver; usually not a clinical problem.

5. Dose in liver disease: No good data available.

6. Comments:

(a) Continued use of drug in presence of early hypersensitivity reactions can lead to progression to more serious symptoms. Accordingly, drug should be discontinued. Some workers feel desensitization can be done successfully.

(b) Occasional hemolytic anemia occurs.

(c) Apparently competes with INH for acetylation, thereby increasing free INH levels.

D. Ethionamide

1. Metabolism by liver: Unknown, but less than 1% is excreted in urine in active form.

2. Liver tissue levels: Same as blood presumably.

3. Bile levels: Data in rabbits suggest 1½x average serum level.

4. Liver toxicity: Occasional toxic or hypersensitivity hepatitis, usually in diabetics.

5. Dose in liver disease: Unknown; close monitoring of renal and hepatic function advised.

E. Pyrazinamide

1. Metabolism by liver: Minor.

2. Liver tissue levels: No good data available.

3. Bile levels: No good data available.

4. Liver toxicity: Toxic hepatitis in 10-20% of patients is dose dependent and usually occurs late (2nd-6th month). It may be fatal.

5. Dose in liver disease: Avoid.

6. Need for careful monitoring of liver functions limits its usefulness.

F. Cycloserine

1. Metabolism by liver: 35% is metabolized at unknown site(s).

2. Liver tissue levels: No good data available.

3. Bile levels: Present, but none reaches stool.

4. Liver toxicity: Not reported.

G. Ethambutol

1. Metabolism by liver: 70-95% is excreted in urine of which 8-15% appears as metabolites. Site of the conversions is unknown.

2. Liver tissue levels: No good data available.

3. Bile levels: Unknown.

4. Liver toxicity: Mild SGOT rise noted in some patients on 25 mg/kg for several months.

5. Dose in liver disease: No change.

6. Comment: New dose recommendation is 15 mg/kg/day in patients on drug over 60 days. This gives adequate therapeutic effect, and avoids ocular toxicity and SGOT elevations.

H. Viomycin

Metabolism by liver is minimal. Very little is known of its metabolism except it is mainly excreted in urine. No liver toxicity reported.

MEDICAL STAFF CONFERENCE

Eosinophilia and Eosinophilic Carditis

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Associate Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. SMITH:* The discussion today relates to eosinophilia. The case presentation will be given by Dr. Homer Boushey.

DR. BOUSHEY:† This 48-year-old Caucasian male was a disabled laborer who was admitted to the hospital for the fifth time on 1 July 1969 for severe chest pain and recurrent shortness of breath. In 1965 tenderness and swelling of the right calf developed and thrombophlebitis was diagnosed. At that time an eosinophil count of 10 percent was noted. The disease appeared to respond to symptomatic therapy; however, after leaving the hospital the patient continued to have painful swelling of both calves and noted weight loss and wasting of the muscles of the legs. Consequently, he reentered the hospital. A muscle biopsy was interpreted as showing acute eosinophilic myositis at a time when the peripheral eosinophil count was 21 percent. The patient first noted palpitations during that stay in hospital.

In 1968 the patient entered this hospital for the first time. Serum levels of "muscle enzymes" were elevated. The diagnosis of eosinophilic myositis was confirmed by a muscle biopsy in which nearly all the inflammatory cells seen were eosinophils.

Screening tests, including upper gastrointestinal series, barium enema, and sigmoidoscopy, were negative. A gastric ulcer was found which subsequently responded to medical management. Cardiomyopathy was also diagnosed on the basis of cardiomegaly, conduction defects, and arrhythmias, including wandering atrial pacemaker and intermittent two to one A-V dissociation.

In September 1968 the patient was admitted to the neurology service for evaluation. On the day of entry he had a syncopal episode and was found to have complete heart block. A pacemaker was inserted which produced good control of the ventricular rate. At that time peripheral eosinophils were only 1.0 percent with an absolute count of only 74 per cu mm. Corticosteroid therapy was started but discontinued because of exacerbation of abdominal pain associated with a recurrent gastric ulcer.

The patient entered this hospital for the third time in December 1968 because of incomplete small bowel obstruction, which responded to conservative management. During this period the patient's congestive heart failure increased in severity, probably as a result of fluid overload. The patient left the hospital and did relatively well with no specific medication for the myositis. He gained weight and generally felt better.

In April 1969 he entered this hospital for the fourth time, because of recurrent shortness of breath. Intermittent failure of the pacemaker to capture the ventricle was noted, and a pacemaker was reinserted with good control of the ventricular response. He continued, however, to have episodic shortness of breath, increasing cardiomegaly, and pleural effusions. A lung scan showed multiple perfusion defects consistent with pulmonary emboli, and anticoagulant therapy was given. Eosin-

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†Homer Boushey, M. D., Resident in Medicine.

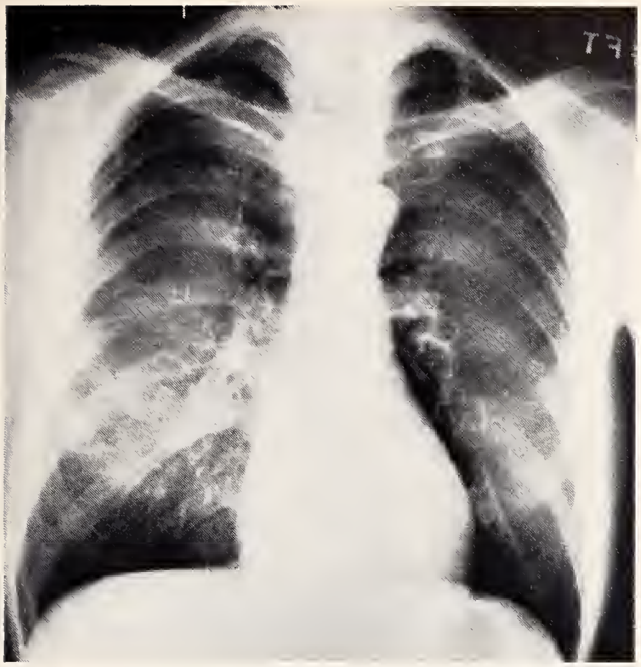

Figure 1.—Radiographic film taken in April 1968, showing normal heart size.

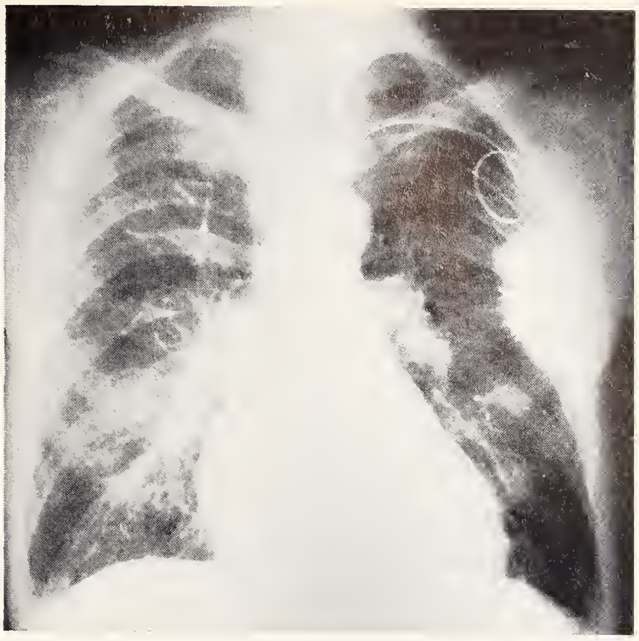

Figure 2.—Radiographic film taken in April 1969, showing increased heart size.

ophils during this admission were never higher than 0.5 percent and an absolute count was 143 per cu mm.

The patient last entered this hospital on 1 July 1969 for evaluation of severe pain of eight hours' duration occurring two days before admission. This pain radiated from the left side of the chest to the right. He had increasingly severe shortness of breath but no cough or hemoptysis.

On physical examination the patient appeared wasted and chronically ill with sunken cheeks and eyes. A livido reticularis pattern was present over the trunk and extremities; the ear lobes were cyanotic. The jugular venous pulse was elevated to 4.0 cm above the clavicles at 30° elevation. The point of maximal impulse was diffusely located over the fifth intercostal space, 1.0 to 2.0 cm lateral to the midclavicular line. A grade ii/vi systolic ejection murmur and a prominent S_3 gallop were heard but no S_4 was evident. The liver was not palpable and there was no pheripheral edema. Pronounced generalized muscle wasting was present with no differential between the proximal and distal muscle groups. Results of neurological examination were within normal limits.

An electrocardiogram showed no important change from previous tracings. Leukocytes numbered 7,000 per cu mm of blood, with no eosinophils. The serum glutamic oxalic transaminase and creatine phosphokinase were elevated as they had been on all previous admissions, presumably because of muscle disease. A lung scan showed considerable clearing since the last admission and no new perfusion defects.

On 3 July 1969 cyanosis and hypotension developed, and a harsh pericardial rub was heard over the entire precordium. Prednisone therapy was begun for the possibility of eosinophilic myositis and pericarditis, but shortly afterward the patient died.

DR AMBERG:* Here is a series of x-ray films beginning 11 April 1968 when the cardiomyopathy was first diagnosed. It is evident that the heart size was completely normal at that time (Figure 1). When he entered the hospital with complete heart block, the heart size was very slightly enlarged. A pacemaker was inserted, and the heart size returned to normal. In April 1969, one year later, the pacemaker failed and the heart size again increased considerably; the patient was in frank congestive failure with much pulmonary congestion (Figure 2). The decubitus film showed free pleural effusion.

DR. SMITH: I suppose now it is unnecessary to introduce Dr. Amberg. We are delighted to have him here representing the Department of Radiology. He is Professor of Radiology and was formerly Chief of the Radiology Department at Fort Miley Veterans Administration Hospital in San Francisco.

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*John R. Amberg, M.D., Professor of Radiology.

TABLE 1.—*Conditions Associated with Eosinophilia*

Drug Reactions	
Examples:	Iodide
	Penicillin
Parasitosis	
Examples:	Trichinosis
	Visceral larva migrans
Infections	
Leprosy	Fungal infections
Brucellosis	
Tuberculosis	Scarlet fever
Malignancies	
Carcinoma:	Lung
	Ovary
	Stomach
Hodgkin's disease	
Collagen Disease	
Periarteritis nodosa	
"Cutaneous"	
Pemphigus	
Dermatitis herpetiformis	
Loeffler's Syndrome	
Farmer's Lung	
Asthma, Hay Fever	
Leukemia	
Chronic myelocytic	
Eosinophilic	
Eosinophilic Endocarditis	(Loeffler's Endocarditis)
?Radiation	
Unknown Cause	
Idiopathic	Cigarette smoking
Sarcoidosis	Tropical eosinophilia

This patient had a very complex illness extending over a four-year period and leading to death with cardiac complications. We have asked Dr. Martin Cline to discuss the patient and the disease entity which this patient represents. We have asked him to focus more specifically on the significance of the eosinophil, its normal function, and the disorders which call forth high levels of this peculiar cell.

DR. CLINE:* Dr. Smith, it is a privilege to be here; it is always flattering when a hematologist is asked to discuss that organ involved in the propulsion of blood rather than the fluid and cellular elements. I shall, however, resist the temptations to discuss the nuances of electrocardiographic abnormalities in eosinophilic carditis. Instead I would like to examine an approach to the diagnostic problem of eosinophilia and to consider where the clinical picture presented this morning may fit into such a classification. Finally I should like to consider the eosinophil itself and its possible pathogenetic significance.

The list of diseases associated with eosinophilia can be gleaned from any standard textbook of medicine and several weeks in the library (Table 1). It is a list familiar to most of you. With your indulgence, I will briefly examine this catalogue in order to place our patient in proper perspective.

Perhaps the commonest form of eosinophilia seen in our hospital at present is that related to drug reactions. Of these probably the most common is sensitivity to antibiotics; although any of a number of drugs may be associated with eosinophilia.[1] The next most common cause of significant eosinophilia seen on our medical service is parasitic infections. The nematodes are the parasites *par excellence* associated with eosinophilia. As a generalization, tissue phases of parasites are much more apt to provoke significant levels of blood eosinophilia than is parasitization of the gut alone.

Visceral larva migrans, as part of the "cat sandbox syndrome," is one of the more interesting causes of parasitic eosinophilia and deserves some comment.[2] This condition is occasionally diagnosed as eosinophilic leukemia. I can clearly remember a small child entering the National Institutes of Health with pronounced hepatosplenomegaly, a blood eosinophil count in the range of 100,000 per cu mm, and a diagnosis of eosinophilic leukemia. Because of the extreme rarity of true eosinophilic leukemia, other diagnostic possibilities were pursued. A liver biopsy demonstrated the typical histologic features of *Toxocara canis.*

Eosinophilia may also be part of a number of infectious processes, including tuberculosis, brucellosis, fungal infections, leprosy, and scarlet fever. It is quite interesting to me to observe some of the names associated with the descriptions of eosinophilia and infection. Franz Ingelfinger,[3] the prominent gastroenterologist and now Editor of the *New England Journal of Medicine,* was one of the first to call attention to the presence of eosinophilia in brucellosis.

Because increase in the number of blood eosinophils is sometimes associated with malignant lesions, an intensive search for the presence of occult neoplasms was made in the patient whose history was presented today. By far the most common malignant change in which eosinophilia is a prominent feature is Hodgkin's disease. In this disorder eosinophil concentrations may reach the level of 50,000 to 70,000 per cu mm. Occasionally eosinophilia is reported in association with carcinoma of the stomach, lung and ovary. From my own experience, I can recall one patient with carcinoma of the lung and eosinophils in the range of 50,000 per cu mm.

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*Martin J. Cline, M.D., Associate Professor of Medicine and Radiology and Associate Director, Cancer Research Institute.

Among the connective tissue diseases, periarteritis nodosa has been most frequently associated with eosinophilia. It is reported that eosinophilia is rare in periarteritis in the absence of pulmonary involvement; with pulmonary involvement, it is quite common. Rheumatoid arthritis may also occasionally be associated with significant blood eosinophilia.

The concurrency of certain cutaneous diseases and elevated levels of blood eosinophils is well known, although the mechanism involved is, of course, quite obscure.

Loeffler's syndrome consists of blood eosinophilia, transient pulmonary infiltrates, and eosinophils appearing in the sputum.[4] Usually the pulmonary infiltrate persists no longer than two weeks; Loeffler himself used the word *fluchtig,* meaning fleeting. The course is generally benign and the cause unclear, although it has been suggested that in some patients the clinical manifestations are the result of the migration of certain parasites through the lungs as part of their life cycle.

Farmer's lung as a cause of eosinophilia is thought to result from the inhalation of mold and a subsequent allergic reaction. The eosinophil may be one of the prominent cells in the acute inflammatory process in this condition.

Association of eosinophilia with asthma and hay fever is, of course, well known. There are some interesting sub-syndromes within these disease categories. At the University of California hospitals two patients were seen recently who had abrupt onset of asthma, fleeting pulmonary infiltrates in an unusual distribution, and a high blood concentration of eosinophils. Both the asthma and the eosinophilia responded dramatically to treatment with adrenocorticosteroids. These patients may have had a recently described disease syndrome, chronic eosinophilic pneumonia.[5] In one of the references which I have given you,[6] there is a notation that patients dying in acute asthmatic attacks may have eosinophilic infiltration of the myocardium as well as patchy myocardial fibrosis. This may have some bearing on what I am going to discuss shortly.

Eosinophilia may be a part of the disease picture of chronic myelocytic leukemia, just as increased blood basophilia is a frequent finding. Eosinophils are rarely the predominant cell in this disorder, but the absolute number of these cells is often increased. I am going to spend most of the next few minutes talking about two diseases: eosinophilic leukemia and eosinophilic endocarditis. The patient presented today may have had eosinophilic carditis. For the sake of completeness, however, I should like to finish my cataloging and then return to these entities.

Exposure to irradiation is said to be associated occasionally with elevated levels of blood eosinophils. One tends to dismiss this association because one cannot readily conceive of the mechanism; however, in my own limited experience I have seen two patients with history of significant exposure to irradiation who had prominent blood eosinophilia. One patient was a technician at the Livermore Laboratories and the clinical manifestations resembled those of eosinophilic leukemia over a course lasting several years.

In Table 1 I have included a category of eosinophilia of unknown cause (not suggesting, however, that we know the cause of the eosinophilia in those diseases already cited). Tropical eosinophilia is a disease characterized by blood eosinophilia and nocturnal cough; it was a significant problem among combat personnel in the Korean War. The cause may be microfilarial parasitization.[7]

Within the category of eosinophilia of unknown origin, there is at least one recorded case of eosinophilia occurring in a patient whenever he smoked cigarettes.[8] Eosinophilia may also occur in sarcoidosis. I found an interesting reference to eosinophilia and "chronic nervous exhaustion" in the *American Journal of Insanity.* Unfortunately that journal stopped publication in the early 1920s, and I was unable to get an adequate follow-up and documentation of this particular cause.

Finally, there is an entity called "idiopathic eosinophilia" which does not conveniently fit into any of the previously mentioned disease categories. The important point to remember is that idiopathic eosinophilia is generally a benign condition. In a good study[9] in which 38 patients with idiopathic eosinophilia were followed, six died during a five-year period—two of chronic myelocytic leukemia, one of carcinoma of the stomach, and the other three of apparently unrelated causes. In general, therefore, idiopathic eosinophilia appears to be without serious pathologic import.

I would like to consider briefly eosinophilic leukemia and whether or not it exists as a disease entity. Until 1960 there were approximately 30 cases of so-called eosinophilic leukemia in the world's literature. This "leukemia" had certain rather peculiar features[10]: In the reported cases anemia as well as thrombocytopenia were somewhat rare. In addition, an extremely high incidence of myocardial involvement was reported, and most of the patients died either of myocardial failure or of peripheral embolization. I believe that most of these descriptions of "eosinophilic leukemia" are actually examples of the syndrome of *eosinophilic endocarditis.* It is likely, however, that eosinophilic leukemia does exist as a separate disease entity; it is, however, extremely rare and considerably less common than eosinophilic carditis. The statement that eosinophilic leukemia does exist is based on the occurrence of the Philadelphia chromosome in a patient with blood eosinophilia, organomegaly, and diffuse organ infiltration with eosinophils.[11] This patient subsequently died in a blast crisis. The entire clinical and pathological picture was quite compatible with that of chronic granulocytic leukemias.

The patient presented this morning was thought to have "fibroplastic parietal endocarditis with blood eosinophils," a disease process described by Loeffler in 1936 in the *Swiss Journal of Medicine.*[12] The major clinical features of the original case were significant: peripheral blood eosinophilia, cardiac failure, and peripheral emboli. At autopsy the patient was found to have fibrosis involving the walls of the heart rather than the valves. Both the ventricular walls and the septum were fibrous, and mural thrombi were present. Since the original report of this entity, there have been approximately 40 cases described. Eosinophilic endocarditis is the usual name applied to the syndrome.

The clinical characteristics of these 40 cases are briefly summarized in Table 2. Although a wide age range has been represented, most cases have been in adults, usually between 30 and 50 years of age and predominantly in males. Almost all the initial reports were from Europe and thus involved a Caucasian population. More recently there have been several cases reported from South Africa involving Negroes.[13] The onset of symptomatic disease has varied from acute to gradual. The duration of disease has also ranged widely from three months to six years; however, I would point out that almost half of the patients died within a year of the onset of significant symptoms. It is a highly lethal disease. Additional manifestations have included central nervous system signs, with seizures being the most prominent feature. Peripheral and pulmonary embolic phenomena have been common. Approximately half of the patients described had a murmur consistent with mitral insufficiency; in the other half the murmur was not clearly defined. There was often a disparity between heart size and the degree of congestive failure, a phenomenon characteristic of constrictive pericarditis. I visualize this disparity as resulting from extensive fibrosis of the endocardium. The course was in general afebrile. Most of the patients had persistent eosinophilia ranging from 30 to 70 percent, but a few were reported as having only very transient blood eosinophilia even though there was eosinophilic infiltrate in organs, including the heart. Electrocardiograms were generally not helpful because they lacked specificity. Only three patients had electrocardiographic evidence consistent with left ventricular hypertrophy. A characteristic feature of the disease entity was a poor response to therapy, including cardiac glycosides and other routine methods of treating congestive heart failure.

TABLE 2.—*Eosinophilic Carditis: Clinical Features in Approximately 40 Patients*

- Age Range
  - 7 to 65 years
  - (Usually 30 to 50 years)
- Male to Female Ratio
  - 3:1
- Population
  - Negro and Caucasian
- Onset
  - Acute or gradual
- Duration
  - 3 months to 6 years
  - (19 out of 40 patients died within 12 months)
- Manifestations
  - Afebrile
  - Eosinophilia
  - Electrocardiogram
    - Nonspecific ST and T changes (16 out of 40 patients)
    - Left ventricular hypertrophy (3 out of 40 patients)
  - Possible embolic phenomenon
  - Murmur of mitral insufficiency (20 out of 40 patients)
  - Possible central nervous system signs
- Therapy
  - Poor response

Eosinophilic endocarditis has a rather characteristic pathologic picture (Table 3): Early in the disease there is evidence of endocardial and myocardial necrosis distributed in a spotty fashion throughout the heart. These early lesions may be

TABLE 3.—*Pathologic Features of Eosinophilic Carditis*

- Early Features
    - Necrosis
        - Endocardial
        - Myocardial
    - Possible small vessel inflammation
    - Cellular infiltrate with eosinophils
- Late Features
    - Fibroelastosis
    - Chronic inflammatory changes

TABLE 4.—*Characteristics of Eosinophils*

- Motile
- Granules
    - Poor in lysozyme
    - Rich in peroxidase
    - Contain protein inclusions
- Phagocytic of Microorganisms
    - (Less phagocytic than neutrophils)
- Phagocytic of Antigen-Antibody Aggregates
- Attraction by Antigen-Antibody Aggregates

accompanied by inflammation of small vessels, and eosinophils are the predominant cellular infiltrate. Near the time of death there are generally extensive fibrotic changes in which both collagen and elastic tissue are involved. In these chronic inflammatory lesions eosinophils may persist, but in general the predominant cell types are macrophages and lymphocytes.

Taken together, the major clinical and pathologic features of the syndrome are

- Refractory congestive heart failure
- Blood eosinophilia
- Endocardial and myocardial fibrosis (usually involving the right ventricle more than the left)
- Frequent mural thrombi and peripheral emboli.

Did the patient presented this morning in fact have eosinophilic endocarditis? The clinical phenomena were consistent with this disease except that eosinophilia was only transient. Among the reported cases, fleeting eosinophilia is extremely rare. The following is a review of the pathologic findings at autopsy: The major pathologic change was limited to the heart which grossly showed endocardial fibrosis primarily involving the right ventricle. Microscopy revealed scattered myocardial fibrosis. In most areas the fibrosis was of long standing, and chronic inflammatory cells rather than eosinophils were present. There were a few areas that appeared to be of recent origin in which eosinophilic infiltrates were present.

I think the patient whose case we are considering today had an unusual variant of eosinophilic endocarditis in that he did not die during a phase of acute blood eosinophilia or of eosinophilic infiltration of the tissues.

I would now like to discuss the eosinophil itself; perhaps what we know of this cell will help to explain some of the pathologic changes or pathogenetic mechanisms of eosinophilic carditis. This is the basic question: Is the eosinophil pathogenic in this disease entity or is it merely an accompaniment of other primary pathologic processes—an epiphenomenon, as it were?

When discussing a similar case two years ago there was only one thing I was very secure about: Eosinophils are red. Since that time we have gained some additional knowledge (Table 4). Eosinophils have crystalline inclusions within their granules. The inclusions are protein, but the nature of the protein is unknown. The granules are poor in lysozymes (presumably they are not involved in the degradation of certain bacterial cell walls) but have a great deal of peroxidase.[14] This peroxidase is chemically and immunologically distinct from the myeloperoxidase of the neutrophil. Human eosinophils are probably rich in antibacterial, cationic proteins, although this fact has not been clearly substantiated. Like granulocytes, eosinophils are motile and phagocytic of microorganisms. They are not, however, either as motile or as phagocytic as the neutrophils.[15]

Two characteristics of the eosinophil which have generated the most attention and speculation are their attraction by antigen-antibody aggregates and their ability to phagocytize such aggregates.[16] Neutrophils are also attracted by antigen-antibody aggregates which have activated certain components of the complement sequence. However, these aggregates appear to be more strongly chemotactic for the eosinophil. The unanswered question is, what is the eosinophil doing to the aggregate or, conversely, what is the aggregate doing to the eosinophil?

In the last few years we have gained additional insight into what the eosinophil may be doing. First, consider the distribution of the eosinophil: It spends most of its life span in the tissues and resides only very briefly (a matter of hours) in the blood stream. Hence the tissue pools of eosinophils are enormously greater than those in the circulation. Eosinophils are found in interfaces; that is, they are found at the body surface in contact with our environment. Eosinophils are abundant on the

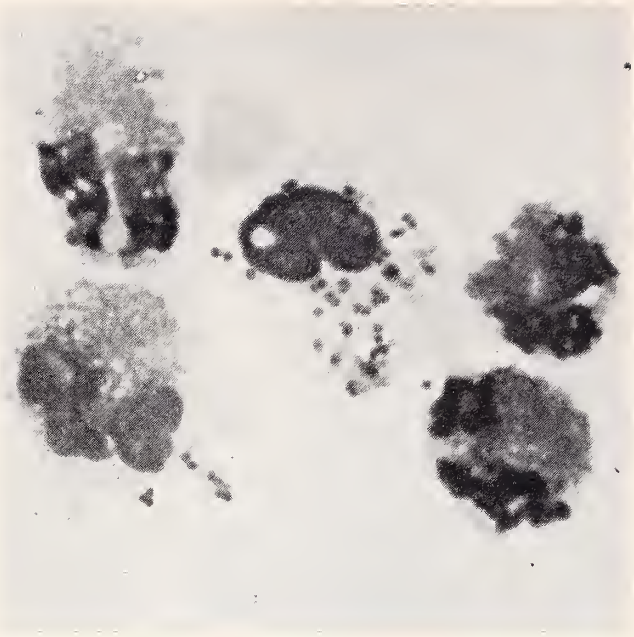

Figure 3.—Neutrophil with many ingested *Staphylococcus aureus* surrounded by comparatively non-phagocytic eosinophils.

gut mucosa, in association with alveolar macrophages at the lung surface, and in the skin. This distribution suggests that the eosinophil may be a first-line defense cell against certain noxious aspects of the environment. Of course, similar suggestions have been made for the lymphocyte in Waldeyer's tonsillar ring and Peyer's patches. It is likely that eosinophils have evolved for a specific purpose rather than being a "phylogenetic carry-over" from more primitive life forms. In all probability, the eosinophil has evolved in higher animals for a specific function which is presumably carried out at interfaces.

In addition, we have noted that eosinophils are attracted by antigen-antibody aggregates. They are not attracted by either antigen or antibody singly but only once the two have formed a complex. The attraction appears independent of the specific antigens involved in the complex and independent of the size of either antigen or antibody. What are the cells doing with these complexes? Clearly they can ingest them; in addition, Archer[17] has published the interesting observation that one can extract from eosinophils substances that antagonize the biological effects of serotonin, bradykinin, and histamine. One may suggest that the eosinophil may be functioning in this regard in order to protect us against the harmful effects of antigen-antibody interactions as well as the pharmacologically active substances generated by such interaction.

The eosinophil is a poor phagocyte in comparison with the neutrophil. I could spend a considerable amount of time documenting this statement,[15] but I would rather show this figure (Figure 3) demonstrating a group of eosinophils and a sole neutrophil exposed to *Staphylococcus aureus.* Obviously the neutrophil, not the eosinophil, has been most effective in ingesting the bacteria. This phenomenon occurs with a number of particles, both bacterial and fungal. The eosinophil simply cannot compete with the faster, more efficient neutrophil.

If the eosinophil is such a poor phagocyte, what then is its function? One observation becomes obvious as one studies eosinophils in tissue culture: With particle ingestion the cell often extrudes its granules intact. One may see intact eosinophil granules circulating in the medium. Is it possible that this granule extrusion plays a role? Is the eosinophil's major function actually not to internalize and digest substances, but rather to release its arsenal into the medium to create an environmental bacteriostatic system or pharmacologic blockade?

In summary, one can consider these possibilities:

- The eosinophil may function to induce bacteriostasis in the environment by extruding its granules, which are rich in cationic proteins and peroxidase.
- Eosinophils prevent tissue injury by antibody-antigen complexes and complement and the associated vasoactive amines and peptides.

What evidence suggests a primary role for these cells in the induction of myocardial fibrosis? To my mind there is no primary evidence that the eosinophils themselves produce tissue injury. All the evidence suggests that they are an epiphenomenon; that is, they are attracted to the sites of myocardial injury which results from another cause. For example, such injury may be induced by a myotropic virus. It is quite interesting that, in an early series of patients with the postmyocardial infarction syndrome,[18] occasionally one had eosinophilia and roughly 20 percent of those patients who came to autopsy had eosinophilic infiltration with spotty myocardial fibrosis. This observation may be one more bit of evidence that eosinophilia is a secondary manifestation of other injuries to the heart.

DR. SMITH: Thank you very much, Dr. Cline. There is time for questions concerning the patient presented this morning or concerning the eosinophil in general.

Martin, could you tell me if other patients have shown evidence of peripheral muscle involvement by eosinophils such as this patient apparently had?

Dr. Cline: The patients described in the literature often had widespread eosinophilic infiltrations involving lymph nodes, spleen, pancreas and other organs. I have not found a specific documentation of myositis extrinsic to the heart.

Question: Have you found any patients who had lesions similar to those in the heart in the capillaries or in the small arteries of the lung? If so, do these lesions resemble those of periarteritis?

Dr. Cline: No, they apparently are distinct from periarteritis. Patients with eosinophilic carditis may have small vessel involvement in the lung, but this involvement generally lacks the typical nodular features of periarteritis. I might say that only some 45 patients are described in the literature; yet we have had two patients with this diagnosis at this Medical Center in the last four years. Therefore, we must be considered an endemic area.

Question: Are the eosinophils in this disease morphologically different from eosinophils in other kinds of eosinophilia?

Dr. Cline: No, it is extremely rare in any situation to see an eosinophil younger than the myelocyte stage of differentiation. Even in most cases of eosinophilic leukemia, the predominant cell is relatively mature.

Question: The patient presented today had an enlarged heart. Is that typical of this syndrome? What was the cause of the endocarditis?

Dr. Cline: Cardiac enlargement has varied. Often a disparity has occurred between the size of the heart and the degree of congestive heart failure, presumed to result from the constrictive nature of the disease. At least one-third of the patients had cardiomegaly, as in Loeffler's original cases. As to your second question, about the cause of endocarditis, I don't know the answer. I might say parenthetically that the coronary vessels of our patient today were totally patent.

Dr. Smith: I gather that with the exception of the presence of the eosinophil, the terminal pathologic features do not differ very much from those of other types of idiopathic fibroelastosis or cardiofibroelastosis.

Dr. Cline: Generally that statement is correct except when one reviews the whole series. The frequent right ventricular predominance of fibrosis in eosinophilic endocarditis is rather unusual. In most types of acquired endocardial elastosis, such as that associated with hypertension, beri-beri, and others, I believe that usually the left ventricle is more involved. The cardiologists may be able to clarify that statement. Pathologically, the only difference between eosinophilic and other forms of carditis is the eosinophilic infiltration.

Question: Is steroid therapy useful in this disease?

Dr. Cline: There is no convincing evidence that it is useful. Steroids have been used in only a minority of cases — those recognized since approximately 1950. Generally the reaction to steroids is a transient or sustained decrease in the blood eosinophil level with no clear-cut, beneficial effect to the patient or to his cardiac function. Apparently steroids inhibit the release of eosinophils or increase their turnover in the peripheral blood rather than interfere with their production.*

**Addendum:* Since this discussion an additional review of eosinophilic carditis has appeared.[19]

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Continuing Medical Education

A Retraining Program for Inactive Physicians

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■ *During the past two years a pilot project was conducted in which 19 inactive physicians were retrained in preparation for resumption of active practice. The initial program consisted of a flexible training program of six months to one year patterned after conventional internship-residency concepts. During the second year the program was modified by providing an initial condensed indoctrination period of two months' duration especially designed for this purpose, followed by a preceptorship type of training.*

The project was considered successful in permitting trainees to enter some form of active medical work, or to enroll in formal specialty training. The observations made by the faculty of the program and its accomplishments are discussed in the light of the effort expended and the cost of the project.

WITH THE PRESENT shortage of medical manpower, which is expected to become more acute in the future, many methods of increasing the physician pool by means other than training physicians in medical schools have been considered. Among those was the retrieval of fully qualified physicians who, for various reasons, are not actively pursuing medical work. The largest pool of such persons is a group of women physicians who, usually for family reasons, left the medical profession. With the encouragement and financial support of the Manpower Division, Bureau of State Health Services, U.S. Public Health Service (later the Physician Education Branch, Bureau of Health Manpower), the Continuing Education Division of the Pacific Medical Center undertook in the Fall of 1966 a pilot project to determine the feasibility of retraining inactive physicians. The purpose of this communication is to report our experiences with this program as well as to suggest means of organizing more efficient future programs.*

Available Facilities

Pacific Medical Center, formerly the Presbyterian Medical Center, occupies the plant that comprised Stanford University School of Medicine before its move to Palo Alto in 1959. It consists of a 240-bed hospital, an affiliated research institute and some ancillary facilities. The hospital had no formal university affiliation until recently, when the Center became a part of the Graduate School of Medical Sciences of the University of the Pacific (Stockton).

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Supported by Contract PH 108-66-207 with the Physician Education Branch, Division of Physician Manpower, Bureau of Health Professions Education and Manpower Training, National Institutes of Health, U.S. Department of Health, Education, and Welfare.

Submitted 20 June 1969.

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*A model of the retraining program can be obtained from the Physician Education Branch, Division of Physician Manpower, Bureau of Health Professions Education and Manpower Training, NIH, Bethesda, Maryland 20014.

However, it has an active educational program: Some departments offer elective courses for senior medical students from the University of California School of Medicine, and accept students from other medical schools as well. Its graduate training program includes internship (20 interns), residencies in internal medicine, surgery, pathology, psychiatry, neurology, obstetrics-gynecology, orthopedics and ophthalmology, and several fellowship training programs. During the past few years all internships were filled through National Institute of Manpower (NIMP) and most of the residency and fellowship positions were filled. In addition, the Center has an extensive postgraduate program and is among the first 14 institutions formally accredited by the American Medical Association's new accreditation system in continuing education for physicians. The hospital staff consists largely of clinical faculty members of Stanford or University of California schools of medicine and includes some 30 geographically full-time teaching staff members.

The Initial Group

The retraining program was initiated in the Summer of 1966 by two of us (A.S. and F.J.S.). The overall supervision of the program was the responsibility of the Director of Continuing Education (A.S.) who selected a faculty member, geographically full-time at the Center (F.J.S.)—an internist who had just completed residency training and a fellowship in cardiology, and who was budgeted to spend 33 percent of her time on the project. In approaching the retraining program, it was realized that this was to be the first formal program of this kind in existence and that there were no precedents as to plan of instruction or curriculum. Several basic decisions were made before the inception of the program: (1) It was to be a practical clinical traineeship of at least six months' duration, with trainees spending preferably full time in training (40-hour week), although provisions have been made for some trainees attending part-time, but not less than 20 hours a week. (2) The core of the training program will be internal medicine, followed by elective brief rotation through specialty services. Only those who have attained board certification or board-eligible status would be given straight specialty training. (3) Trainees were not to be given primary patient responsibilities and were exempt from after-hours and night "on-call" service.

Recruitment

A list of women physicians not in practice was obtained through the Bureau of Research and Planning of the California Medical Association from the master tape of the AMA. The list revealed 67 such persons within the San Francisco Bay Area counties (population 4.6 million). Each physician in the area on the list received a letter-questionnaire asking whether such a training program would be of interest to her. Forty-five answers were received, 33 expressing interest. A follow-up letter sent to the 33 interested women described the proposed program and indicated readiness to accept applications. Six women physicians indicated willingness to start training at once. They were interviewed, were found acceptable, and constituted the first class of trainees. Two more enrolled later during the first year.

Analysis of the trainees

The first class, which began training in September 1966, consisted of eight students, ages ranging from 39 to 57, who had been away from training or active practice for five to twenty-two years. All trainees were married (two widowed). Six of the eight had children. Ages of children ranged from 18 months to adulthood, family size from one to five children. The original graduate training of the candidates ranged from completion of internship (one) to board certification (two, a pediatrician and a radiologist). Graduate training included rotating internship and residencies in internal medicine, anesthesiology, psychiatry and surgery, in addition to the certified specialists.

Planning and initiation of the program

Before commencement of the training program the objectives and plans of training were discussed in detail with the chiefs of services and members of the house staff. The background and estimated amount of guidance the trainees would need were discussed. The hope was expressed that the interns and residents would participate actively in the teaching program. It was made clear that the addition of the trainees to the ward staff should in no way infringe on the teaching opportunities of the house staff. The program, when presented in this fashion, met with interest and enthusiasm by the attending and the house staffs alike.

Each new trainee was met with individually to discuss prime objectives of retraining. With the information thus obtained, we tried to design individual programs which would fit best the needs and objectives of the trainee.

Early in the training, both the trainees as well as the supervisors recognized the limitations imposed by prolonged absence from practice as well as differences in background, age and future plans. Necessity for more intensive training in limited fields also became apparent. The two board-certified specialists were trained in the respective fields. The pediatrician had exclusive retraining in pediatrics; arrangements were made to provide her with training in other institutions than our own in those areas of pediatrics where our material was inadequate. The radiologist obtained retraining full-time in the department of radiology, but at her own request was included in general training in internal medicine for a period of one month.

A third candidate had four years of training in general surgery but lacked one more year for completion of her training. She spent her initial two months in the department of medicine and then the remainder of her time in orthopedic surgery (as a possible step toward formal training in this field in the future). Candidates who were not sure about the type of medical work they might wish to do in the future were assigned to the department of medicine and were initially given ward service training. Five trainees started their rotation on the medical wards. Three of them, two with background of general practice and one of internal medicine, planned to resume practice in offices or hospital outpatient clinics dealing primarily with adult patients. Their rotation, after exposure to internal medicine, included such outpatient clinics as gynecology, dermatology and otolaryngology, as well as rotation through the Emergency Room service.

The fourth trainee had worked in the past in an emergency hospital and wished to resume similar work. Her training included internal medicine, followed by assignment to the Emergency Room. The fifth trainee had worked as an anesthesiologist up until about 20 years before commencement of retraining. Her objective was to work in gynecological office practice, for she developed interest in that field. Her training included internal medicine, followed by prolonged assignment in the gynecological clinic.

All trainees were required to attend the formal teaching sessions for the house staff (teaching conferences in the various specialties, basic science lectures, clinicopathological conferences, tumor boards and the like), and were encouraged to attend postgraduate conferences given by this institution which took place two to three times a month, usually on Saturdays. Arrangements were also made to admit the trainees to suitable postgraduate courses offered by the University of California School of Medicine, San Francisco. In addition, a series of lectures designed specifically by the trainees were given by staff members of this hospital. A list of recommended reading, consisting of texts and review articles, was given to trainees.

Changes in Curriculum

The first year's curriculum was considered experimental and observations concerning its effectiveness were made continuously. The initial curriculum was designed along conventional lines of graduate medical education—that is, a modified internship-residency type of retraining. The advantages and disadvantages in utilization of this system became apparent within the first few months of the training program. On the positive side, inactive physician-trainees constituted a well-motivated, knowledge-hungry group of students who on the whole were more mature than the average intern and resident. Absenteeism was virtually non-existent, and attendance at voluntary teaching sessions, such as weekend courses for practicing physicians, was very high—a decided contrast with the house staff. On the negative side, most trainees had an initial lack of confidence; there was a reluctance to assume responsibility for patients. A need for a more systematic review of material once learned—physical diagnosis, differential diagnosis, use of laboratory tests and modes of treatment—also became apparent.

On the basis of our experience with the first class, the following new curriculum evolved for the second year of our project. An initial indoctrination period was organized, during which didactic instruction specially designed for this group was given. "Headquarters" were developed, namely a combination conference-study room for these special students. A half-time coordinator was recruited among graduates of the first class (M.B.). A systematic review of newer modes of diagnosis and treatment was developed and consisted of lectures, roundtable discussions, and teaching films and tapes. Orientation in ancillary hospital services—social service, nursing, medico-legal matters, physical and occupational therapy—was included. In addition, a small library of books and reprints, specially designed for the re-trainees, was housed in their conference room.

The second class began in October 1967 and included five trainees, plus one carry-over trainee from the first class (she had begun her training late during the first year). The new group included one man who had been away from medical work for a number of years. Ages of the new students ranged from 30 to 60 years; graduation dates 1936 to 1962. Time away from practice ranged from five to twenty years. Individual rotation, taking into account earlier training and future objectives, was applied to this group, as to the first one. In January 1968, budgetary cuts of the USPHS contract required a reduction of the trainee stipends to one half. This was accepted readily by all trainees. In May 1968, a third class was initiated for a four-month training course (five trainees). This group received no stipend at all. The curriculum followed closely that developed for the second class.

Follow-up

Of the initial group of eight trainees all obtained medical positions as follows: two work in a medical office—a surgeon and a gynecologist; two are full-time physicians in a hospital out-patient department; the two specialists resumed specialty practice—radiology and pediatrics; one enrolled in a residency in physical medicine and rehabilitation at a medical school and one works for the State Welfare Department.

Discussion

This training program, in addition to offering 19 persons the opportunity for reentry into medical work or updating their knowledge, permitted us to review at first hand the needs of such a group and to visualize the kind of program which would be ideally suited to fill these needs.

It should be realized, first of all, that medical re-trainees constitute a widely heterogeneous group of persons with wide variation in personal motivation, background of knowledge, age, physical stamina, length of previous training and time away from practice. It is clear that the existing conventional training programs, such as residency or postgraduate courses, are seldom suitable for such persons, at least initially. Flexibility in the total program appears to be an important prerequisite of a successful program. It is our impression that a curriculum specifically designed for such persons is imperative. Such a curriculum should consist of two phases: Phase 1, an intensive review course in basic aspects of clinical medicine; Phase 2, a program of supervised patient contact with gradually increasing assumption of patient responsibility. The first phase belongs in a major medical center—either a medical school or an institution with an active postgraduate program. Such an institution, in undertaking a program of retraining, should devote enough thought, funds and energy to work out a specially designed program, rather than attach it to existing teaching functions. The second phase might be undertaken by a smaller teaching hospital, provided its faculty has the motivation and understanding of the problem involved in conducting it.

The recruitment of students requires careful planning. Our experience indicates that a direct approach by letter or questionnaire of the pool of inactive physicians provides a small yield—less than 10 percent. In selecting the candidates for retraining, the most important points appear to be the psychological makeup, adequate general health, and assurance of plans to assume some medical work. It is important to note that the great majority of candidates for retraining are geographically tied to an area by virtue of a husband's job and responsibility; and many have home responsibilities that make part-time programs preferable. Our experience had demonstrated that availability of stipends, while not a prerequisite for enrollment, does constitute an important inducement, particularly for those whose standard of living makes the addition of a housekeeper a financial hardship. Therefore, availability of selective, rather than routine, scholarship funds appears to be highly desirable in initiating such a plan.

The expense of running such a program is considerable. In the first place, trainees are unlikely to be able to pay tuition—they may even need subsidy. Secondly, the program is too complicated to be run by volunteer faculty. Our program provided funds for a coordinator who devotes one-third of his time to the job and who later was assisted by a half-time instructor. In addition funds are provided for a modest number of lecture honoraria. Such a core faculty was adequate for a demonstration project, but would have to be enlarged, if a continuous, routine program were in existence.

The initial phase of retraining—the re-indoctrination phase—may be condensed into an intensive course of six to eight weeks. As was previously stressed, such a course belongs primarily in a major medical center, preferably in an institution with major interest in continuing medical education. While such courses would be primarily designed for the reactivation of physicians who have been away from medical contact, it could also be used with some modifications for updating practicing physicians. Whether such courses were to be given once a year, or at more frequent intervals, would depend on the number of applicants. It would probably be most economical to have not more than four or five such courses given at widely scattered geographical locations over the West Coast, Midwest, East Coast and the South in areas where the largest pool of inactive physicians is known to exist. It is assumed that such a short course could be attended by a woman physician some distance from home in spite of family obligations, provided that a longer retraining of Phase 2 would then be found in a location near her home. Such a course could be sufficient to prepare those trainees who so desire, to enroll in a formal residency training in lieu of the specially designed Phase 2 of retraining. Such formal training would be made more attractive if a half-time residency (one year of training extended to 24 months) were made available. Such a plan has been experimented with in some fields in the Boston area in response to a pilot study by the Radcliffe Alumnae Association.

Perhaps the most important question related to the project is whether the expense and the effort of organizing such a program is worthwhile. Our study has shown that only a small fraction of potential candidates for retraining took advantage of the offer—even with the inducement of financial support.

Undoubtedly, the more strongly motivated retrainees would have found other means for returning to medical work. Nevertheless, a program especially designed for such a purpose by individuals who have given a great deal of thought to the program unquestionably increases the probability of producing a better end-product. While the most obvious pool of inactive physicians is women who have family obligations, other members of the medical profession could also be retrained and become better prepared for active medical work. Among the latter are physicians who retire from the Armed Services Medical Corps and who spend some years in medical administration, those who interrupted medical work for reasons of health or those who may have had their medical license temporarily suspended. Furthermore, such programs may be more suitable for many foreign-trained physicians aiming at settling in this country than an internship at a hospital with minimal teaching facilities. Finally, it should be pointed out that in some European countries, entirely independent postgraduate schools of medicine have been very successful, such as the Royal Postgraduate Medical School of the University of London. Postgraduate institutions have, generally, not been too successful in our country. This program may be more suitable to a postgraduate school than a medical school, whose major responsibility is to train undergraduate students and provide graduate training programs.

EDITORIAL

Professional Liability And Patient Care

The escalating cost of professional liability insurance which practicing physicians in California must bear reflects a situation which can only have profound effects on the quantity, quality and cost of patient care. The problem is underscored at this time by the fact that thousands of physicians had their premiums a little more than doubled, beginning first of October, and for some specialists these premiums amount to several thousands of dollars a year. The number of malpractice suits is increasing, the costs of litigation are rising, some of the awards are becoming astronomical (there are several over a million dollars), and quite understandably there is a notable lack of enthusiasm in the insurance industry to rush into this sort of business, particularly when carriers have no sure way of knowing how long after an incident a suit may be filed or what the going rate for awards may be when it is settled.

The causes of all this are complex. Physicians know that there is a risk of untoward reaction or a poor result in almost everything they do, no matter how well they do it. It is true that as science advances and new and better treatments become available, these are often more dangerous and carry greater risks. Yet when an unfortunate result occurs, the courts are apt to hold "the thing speaks for itself" *(res ipsa loquitur)* and the defendant physician finds himself in the factual position of being guilty unless he can prove himself innocent, which seems somewhat unfair in these days when the presumption of innocence for even the manifestly guilty is so high on the legal agenda. There also seems to be a growing feeling abroad that everyone has a right to be healthy, that medical science now knows enough to make everyone healthy, and that when there is a failure it must be someone's fault. Experience shows that this approach can be costly. The traditional reluctance of patients to sue their physicians and the erstwhile reluctance of juries to hold the physician responsible when an unfortunate incident occurs, because he "tried to do his best," is becoming a thing of the past. We are living in a new era when the right to sue is being fully exploited by the public. One can only speculate concerning how much the peculiarly American custom of contingency fees for plaintiffs' attorneys may have to do with it.

There is no question that when a physician truly commits malpractice the unfortunate patient should receive fair compensation insofar as this is possible. This is the position of the medical profession, which long ago took steps to make qualified disinterested physicians available to testify in behalf of plaintiffs and so negate the so-called "conspiracy of silence." Through the mechanism of review and advisory committees medical societies have sought to determine if malpractice was actually committed as the plaintiff claimed, and, if there was malpractice, recommend that the suit be fairly settled, and if there was no actual malpractice that it be fought. There have also been many programs to reduce the causes of malpractice and of suits, the most recent being the highly successful "California Invitational." For several years the California Medical Association has sought relief through the Legislature, this in the public interest as much as for the physician. The first successful effort resulted in the "Good Samaritan Law," and other bills subsequently enacted have extended the principle of this law. Last year the Legislature passed several new laws dealing with the statute of limitations, privileged communications for medical society and hospital staff committee proceedings and records, and advance payments to an injured patient, without presumption of guilt, all of which were helpful. An experiment is being tried with prior agreement to use arbitration. There is talk of something like "trip insurance" whereby insurance against a bad result would be purchased by the patient at the time of each hospital admission. There is discussion of a possible limitation on the extent of the professional liability of physicians, as is now the case with the liability of employers in industrial accidents. And it is intended that independent actuarial analysis will be sought of the underwriting experience, claim and loss projections and premium structure of all the principal professional liability carriers in the state, as has already been done with some.

But the escalating costs of professional liability insurance continue to race ahead of all these worthy efforts to control them. The impact upon the quality of patient care and its cost is now becoming serious. On the positive side there is no doubt that the ever-present threat of suit has tightened up many procedures and practices. But it has also led more and more to what has been called "defensive medicine," that is, those things a physician does or does not do in order to lessen his risk of being sued. The things the physician *does,* in this regard, often unnecessarily increase the cost of health care, and those he does not do may well deprive a patient of an opportunity to receive the latest and best in scientific care simply because the risk is more than negligible. Also on the negative side, it is obvious enough that all the costs of litigation and awards are ultimately paid by the public, although this basic fact is accepted reluctantly or not at all in some quarters.

In a larger sense some of the predictable effects on health care delivery may prove even more serious. For example, young physicians may begin to seek alternatives to starting in private practice because of an unbearably high cost of the professional liability insurance which they must have even before they can see a patient. And, even worse, what will be the action taken by physicians already in practice if the cost becomes prohibitive or if they are no longer able to get any insurance at all? This would mean that they would have to assume a personal risk of an adverse court judgment which might be for a million dollars or more. This is not mere speculation. There is already good evidence that a substantial number of physicians are beginning to take shelter from these problems, from the irritants of government interference with their practice and from other deterrents to fulfilling a personal direct responsibility for a patient's care, which is the very core of private practice. These physicians, often among the most capable, are seeking other avenues for their professional fulfillment. The lesson is too slowly being learned in a number of quarters that physicians are very much like other people. They go where the incentives are and avoid the deterrents.

The eventual effect of all these current trends upon the quality and quantity of patient care is impossible even to estimate. The forces described are among the many which could easily lead to the destruction of personal direct physician responsibility for individual patient care. It is hard to guess what the ramifications of this might be for the profession or for society, but it is equally hard if not harder to imagine how in the world the patient might ultimately benefit. The medical profession is doing all it can. Perhaps the time has come to give it some real help.

Management of Diabetic Coma

THE ARTICLE BY Gwinup and Steinberg in the current issue of this journal (page 347) treats an old subject in a modern way. A few points brought out by these authors deserve some additional comment.

Whereas diabetic coma was the first cause of death in persons with diabetes before the advent of insulin in 1921 and practically always terminated the lives of juvenile diabetics, any fatal outcome today must be attributed either to complicating factors or inadequate therapy. There is, unfortunately, still too much of the latter, as suggested by the variation in mortality figures of 25 to 2 percent in different reports.[1] This is chiefly referable to poor therapy and the differences in know-how between one group and another.

Many cases of diabetic pre-coma are really "intercurrent ketoacidosis" and are found frequently in insulin-dependent diabetics, being most prominent during the teen age. These patients are easily handled by readjustment of their insulin and being careful to continue carbohydrate intake, if anything at a higher level, and if necessary by vein, since inadequate utilization of glucose invariably leads to mobilization of free fatty acids and subsequently to acidosis.

The more severe cases of diabetic coma, however, are those accompanied by CO_2-combining power below 15 mMoles of CO_2 per liter. At this level pronounced drowziness is observed but coma does not usually ensue until levels below 10 mMoles per liter are reached. One then deals with coma.

The first duty of any physician is to *prevent* diabetic ketoacidosis and coma. Most often the patient's self-neglect is at the root of the trouble; he may omit his insulin, starve, or fail to deal adequately with undue metabolic stresses such as annoying experiences, anxiety, infections, and severe trauma. All of these require increased insulin intake. It is the education of the patient and family on how to avoid these preludes to diabetic coma that is all-important. Most often this is left to ancillary personnel such as nurses, social workers, and neighborhood friends who do not always do justice to this all-important precautionary matter.

Once typical symptoms have appeared, there is too often a *delay* in diagnosing and initiating treatment. Every case of severe diabetic ketoacidosis with impending coma must be considered an emergency and the patient admitted to hospital for immediate treatment in the emergency room and continuous monitoring.

As pointed out in the article, the *diagnosis* can be made promptly by the use of bedside procedures such as Dextrostix® (Ames) and Acetabs® (Ames). However, one must then draw blood for baseline determinations in the clinical laboratory before starting therapy. Normal ketone bodies with a high blood sugar are characteristic of the relatively recently described syndrome of *nonketotic hyperosmolar coma,*[2] treated with much insulin and hypotonic fluids of neutral pH. In contrast, normal ketone bodies with only moderate, if any, elevation of blood sugar, but with signs of pronounced acidosis (such as deep hyperventilation) point to *lactic acidosis,*[3] requiring treatment with bicarbonate. In addition to determining glucose levels and ketone bodies at the bedside, a complete blood count, preferably with a hematocrit, is necessary for evaluation of hydration during treatment. One should not be led to assume that there is severe infection by finding leukocyte counts above 12,000 per cu mm of blood with a shift to the left in the differential. This is part-and-parcel of ketoacidosis per se. An electrolyte panel and electrocardiogram before therapy are essential. A serum creatinine determination is useful for evaluation of the degree of renal impairment, often quite reversible.

Insulin therapy consisting of crystalline insulin must be started immediately and vigorously. The intravenous route is preferable to subcutaneous at first, especially if there is a degree of shock. With a severe coma, 100 units must be given half-hourly. The induction of hypoglycemia at the onset is practically impossible. In contrast, giving insulin "too little and too late" has accounted for many a fatality.

For *shock* one often uses albumin, and rarely one must use blood as well as large amounts of 0.45 percent saline solution. This is used rather than 0.9 percent isotonic sodium chloride solution since these patients are decidedly dehydrated and hyperosmolar. Next, one must concentrate on improving the prevailing *acidosis,* which may be inferred from the low CO_2-combining power or by finding a decreased pH. Ordinarily this will be below the normal of 7.4 and closer to 7.0. Since the action of insulin is decidedly impaired by the acidosis, it behooves one to raise the pH into the range of 7.3 to 7.4. This cannot be achieved promptly by the use of 1/6 molar sodium lactate since it must be metabolized before the sodium becomes readily available. The same is true of sodium chloride, which can counteract acidosis only after the chloride has been excreted into the urine; this takes time and good kidney function. Thus, it is preferable to use sodium bicarbonate, adding one to three vials of 44 mEq each to the 0.45 percent sodium chloride infusion. One cannot overemphasize the need to start adding *glucose* to the intravenous fluids as soon as the blood sugar level has reached between 200 and 300 mg per 100 ml. This will allow for the reduction in ketone bodies which insulin alone cannot do effectively. Soon afterward, *potassium* must be started in the form of 20 to 40 mEq per liter as potassium chloride or preferably basic potassium phosphate. The former is slightly acidifying; the latter acts as a buffer and supplies both potassium and phosphate, which are used in the deposition of glycogen in the liver and in the utilization of glucose in the periphery. The failure to add potassium to the regimen may result in a fatal vascular collapse after eight to twelve hours of therapy, due to cardiac arrest.

It is most important for adequate therapy of diabetic coma to be aware of the danger points that might lead to a fatal outcome. Acute *gastric dilatation* may be dealt with by evacuating the stomach, and lavage with sodium bicarbonate before starting insulin therapy. An *inadequate dosage of insulin,* especially when given subcutaneously rather than intravenously with the patient in shock, leads to central nervous system depression and either continuation or recurrence of coma. *Sudden cerebral edema* during therapy is particularly likely to occur when a fall in blood sugar and a rise in pH have been induced too rapidly. This is found to be accompanied by atrophy of the central nervous system due to anoxia and the changes in the extracellular fluid composition. In general, when the blood sugar level in the plasma and extracellular fluid is lowered, it leaves the cerebrospinal fluid glucose still elevated, and this will lead to increasing edema of the central nervous system. An abnormal pathway for glucose metabolism in the CNS leading to sorbitol deposition has recently been implicated as another causative factor. Finally, *hypokalemia* with cardiac irregularities and arrest is a late complication that can be completely prevented by giving potassium. However, one must guard against starting this too early, since usually at the very onset of diabetic coma, especially with acidosis, there is an elevation of serum potassium and adding more can lead to cardiac arrest with hyperkalemia. Lately a few cases of low potassium at the onset have been described[4]; they are very rare. Fortunately, the electrocardiographic changes between these two extremes are quite different; thus, one can differentiate even before the laboratory determinations for potassium are available.

To assure a favorable outcome of diabetic coma, one must consider the therapeutic attack at three levels: First, one must control shock and dehydration. Second, one has to rapidly reduce ketoacidosis and hyperglycemia. Third, one has to be aware of secondary *hypo*kalemia and rarely hypoglycemia. There is a finite mortality, even now. The total prevention of this occurrence can be achieved only by careful, repeated education of the patient and family. They must be warned never to forego the insulin injection, while providing (if necessary) carbohydrates by small sips of sugar-sweetened tea or fruit juices between attacks of nausea and vomiting. In this fashion, the worst type of ketoacidosis can be prevented. Since therapy has to be rapid to be effective, one should prepare for this emergency by having the insulin and the different solutions readily available for a day that we hope will never come.

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Phlebotomy Treatment Of Porphyria Cutanea Tarda: Is It Really Effective?

PORPHYRIA CUTANEA TARDA (PTC) is the most commonly recognized form of porphyria. The term *porphyria cutanea tarda* was first offered by Waldenstrom in 1937[1] and included all forms of porphyria with cutaneous lesions other than congenital porphyria (Gunther's type). It was not until 1954 that Schmid, Schwartz and Watson[2] proposed that a "cutanea tarda type" of porphyria without any other manifestations be recognized. At about that time, reports from England and South Africa emphasized the constant high fecal excretion of protoporphyrin and coproporphyrin in many patients with cutaneous porphyria, and currently the term *variegate porphyria* is applied to that familial type of porphyria with both cutaneous disease and acute porphyria attacks. Porphyria cutanea tarda, on the other hand, is a purely cutaneous disorder, characterized by a pronounced increase in urine and fecal uroporphyrin of hepatic origin, no increase in urine porphobilinogen and, in contradistinction with variegate porphyria, fairly normal fecal protoporphyrin excretion.

Most of the earlier descriptions of PCT emphasized a high frequency of frank liver disease, usually alcoholic cirrhosis. A larger experience, however, now indicates that cirrhosis is not common among PCT patients. Eales noted abnormal BSP retention in only 23 percent of PCT subjects in Cape Town.[3] In our own experience, cirrhosis has been present in fewer than 10 percent of patients. On the other hand, a fairly heavy intake of alcohol is common.

Until the early part of this decade, no treatment, other than interdiction of alcohol, was being seriously offered to the PCT patient. Following the initial communication by Ippen, in 1961,[4] a number of enthusiastic reports have now appeared relating remission of PCT to repeated phlebotomy. This therapeutic approach followed the recognition of frequent high values for plasma iron and hepatic siderosis in PCT patients. Elsewhere in this issue (page 357) there is an additional report by Dr. Herschel Copelan, suggesting that remission in a PCT patient was induced by the removal of 4,600 ml of blood over a period of five months. It is always hazardous to draw any conclusion from a single case therapeutic experience but a sufficient number of cases treated by phlebotomy have now been reported to be impressive. If phlebotomy treatment for PCT is effective, the reason for its effectiveness is not so clear.

An overwhelming amount of evidence is available demonstrating a high incidence of hepatic siderosis in PCT patients. Descriptions of liver biopsy material, reported from many parts of the world, have shown excess iron in both parenchymal and Kupffer cells in nearly 75 percent of PCT subjects. Elevated values for plasma iron and, more particularly, saturation of circulating transferrin are also commonly observed. As pointed out by Kalivas et al,[5] the degree of hepatic siderosis, when present, although variable, is usually not pronounced and is more of the order observed in alcoholic cirrhosis with hepatic siderosis than that observed in classic haemochromatosis.

In many patients, the iron overload may be related to the heavy alcohol intake. In some patients who have consumed no alcohol, a history of heavy iron ingestion, usually as an iron-containing vitamin preparation taken over many years, can be elicited. Among Bantu subjects in South Africa, PCT is common and hepatic siderosis is also common, presumably from drinking the notorious "Kaffir beer," containing large amounts of iron. We and others have observed PCT with hepatic siderosis in elderly men receiving estrogen therapy for prostatic carcinoma. Welland and Carlsen reported an eight-year-old boy with "PCT" and hepatic siderosis who had taken oral ferrous sulfate for two years.[6]

In spite of the frequency with which hepatic siderosis is observed in association with PCT, any causal relation between hepatic iron and hepatic uroporphyrin synthesis has not been demonstrated. For example, patients with classic haemochromatosis or alcoholic hepatic siderosis do not show any evidence of disordered uroporphyrin metabolism. PCT has traditionally been considered to be an acquired disorder with an idiosyncratic background and it is possible that against this idiosyncratic background, environmental factors, such as iron, alcohol and estrogens, either alone or in combination, may precipitate the disorder of uroporphyrin metabolism. In this light, the report by Welland et al[7] of PCT in one of identical twins is of interest. Only the involved twin had taken oral iron and showed excess iron in liver biopsy tissue. Also, we have observed PCT to develop in a patient with a refractory anemia after he had been heavily transfused and had acquired pronounced hepatic siderosis.[8]

Quite obviously, it has been attractive to attempt to treat a disorder so frequently associated with iron overload by phlebotomy; and many reports, including Copelan's current case report, describing remission following repeated phlebotomy, have now appeared. As is so often the case with a new therapeutic approach to a problem, it is disappointing to recognize that no investigator has seen fit to subject phlebotomy treatment of PCT to a controlled trial. This critique is particularly germane to PCT since biochemical and clinical remission can well occur without phlebotomy, especially in the alcoholic patient who stops drinking. Nevertheless, it is impressive to observe virtually complete biochemical remission following the removal of 2,000 to 4,000 ml of blood in a patient who has had PCT for a number of years.

If phlebotomy is an effective treatment for PCT, the question that must then be asked is how it works. It is probably deceptively logical to assume that the simple removal of iron from the liver affects hepatic uroporphyrin metabolism. It should be reemphasized that not all patients with PCT have evidence of iron overload or hepatic siderosis. Nonetheless, such patients also appear to benefit from venesection. Protracted remissions have been observed in a few PCT patients who had received chloroquine, and liver biopsy specimens during remission showed the same degree of hepatic siderosis as before the chloroquine was given. If the effect of phlebotomy is not related to iron removal, then one can only speculate as to alternate mechanisms. Certainly it is unlikely to be the removal of porphyrin, per se, since the amount of porphyrin withdrawn in the course of often repeated phlebotomy is minute compared with the uroporphyrin excretion in a single day. Other factors, critical to the abnormality of uroporphyrin metabolism characterizing PCT, might be removed during phlebotomy and might be very slow to reaccumulate, particularly if predisposing influences such as alcohol were also then discontinued. It should be pointed out that when alcohol, estrogens and iron ingestion seem to be related to PCT, there is invariably a long history of this exposure, usually years, before clinical PCT develops. In this sense, it is of interest to note that with continued alcohol intake the patient reported by Copelan did have a striking increase in uroporphyrin excretion again, three years after the phlebotomy treatment.

The uniformly good response to phlebotomy among PCT patients probably attests its validity even though a controlled trial has never been done. However, the mechanism for this effect remains unclear in spite of the superficial evidence that iron removal is involved. A controlled trial, randomizing patients for removal of only red cells versus removal of only plasma, might well answer some of these questions.

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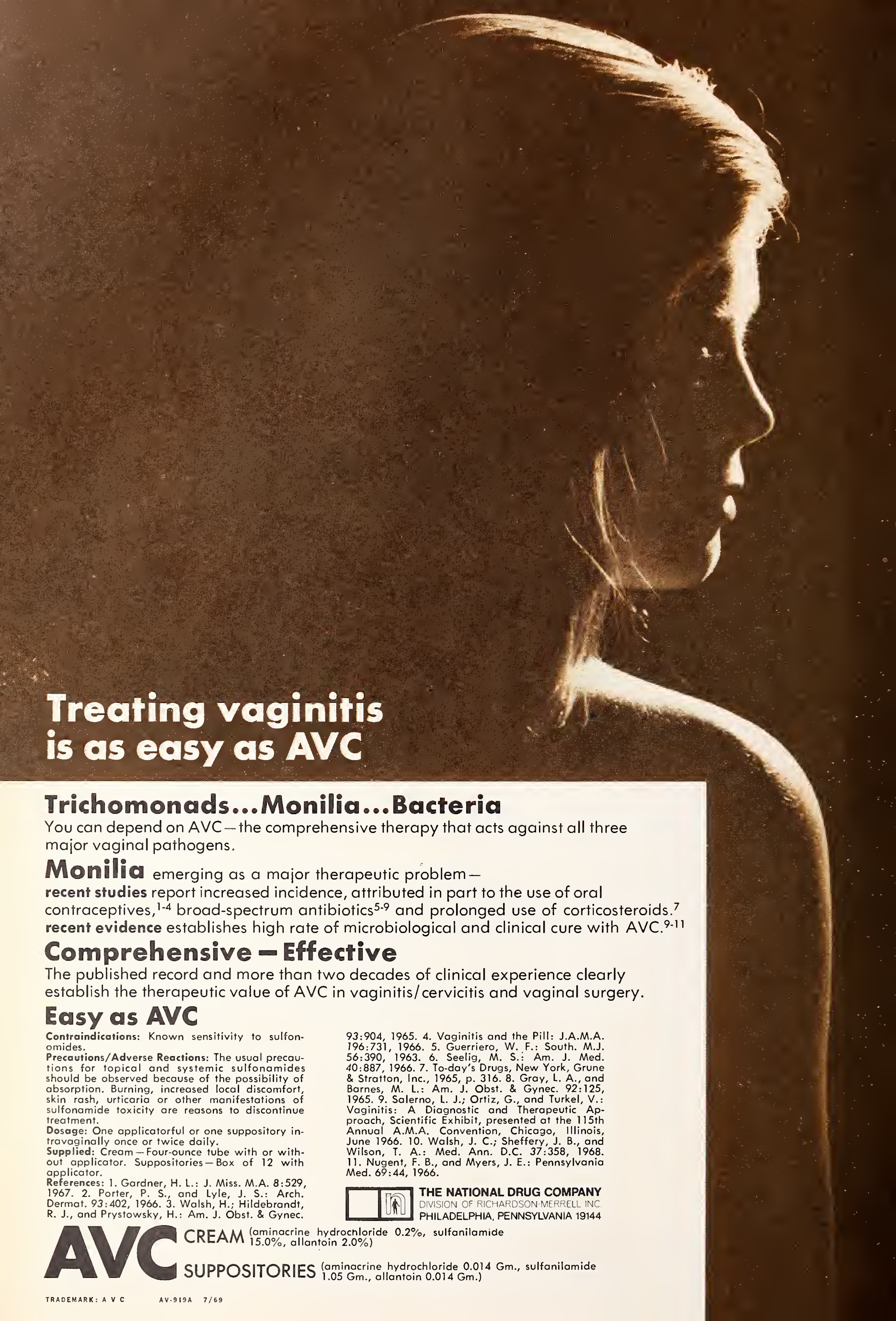

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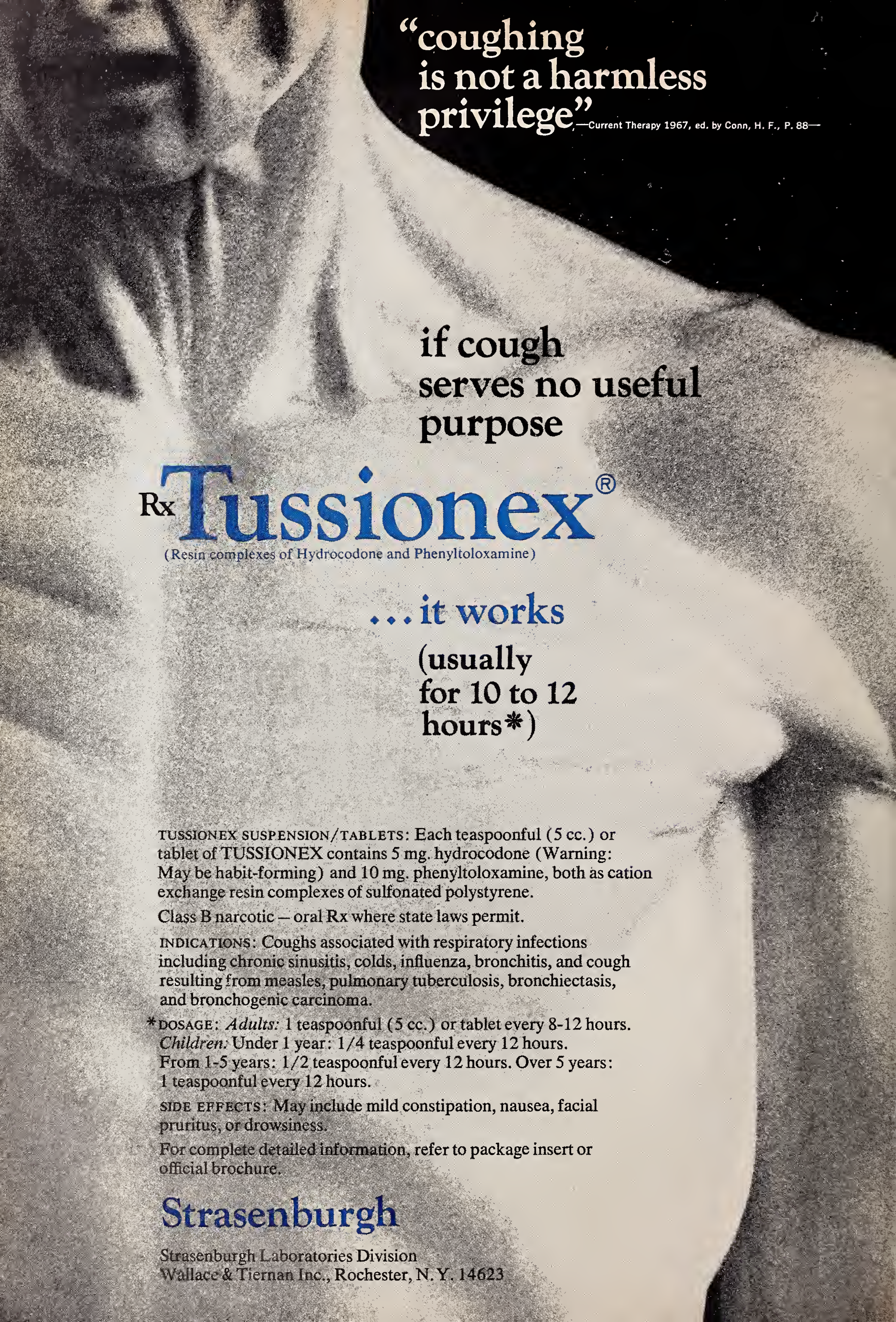

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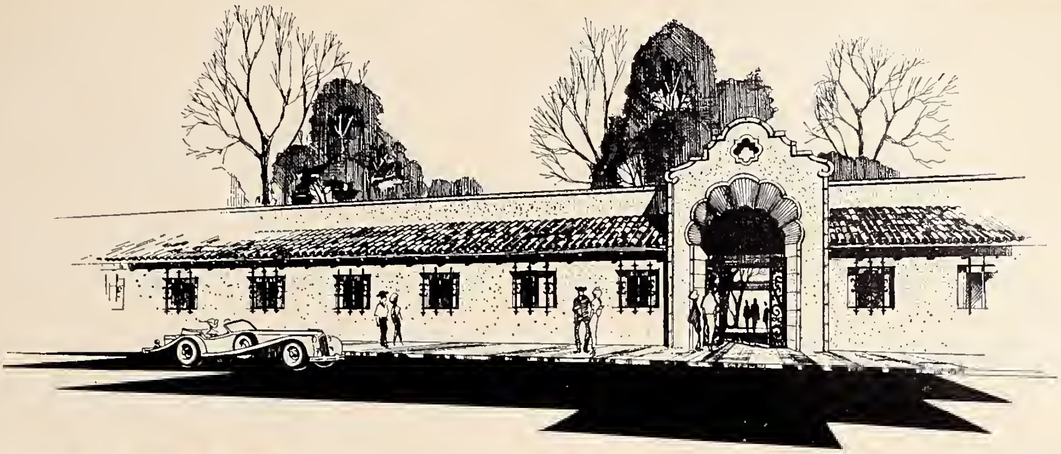

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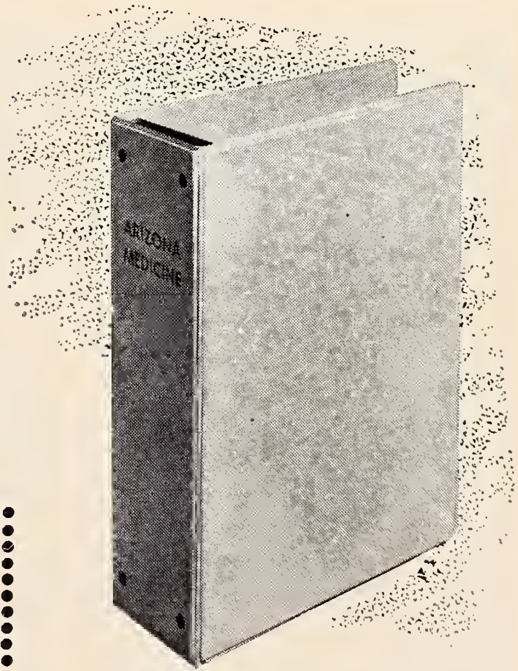

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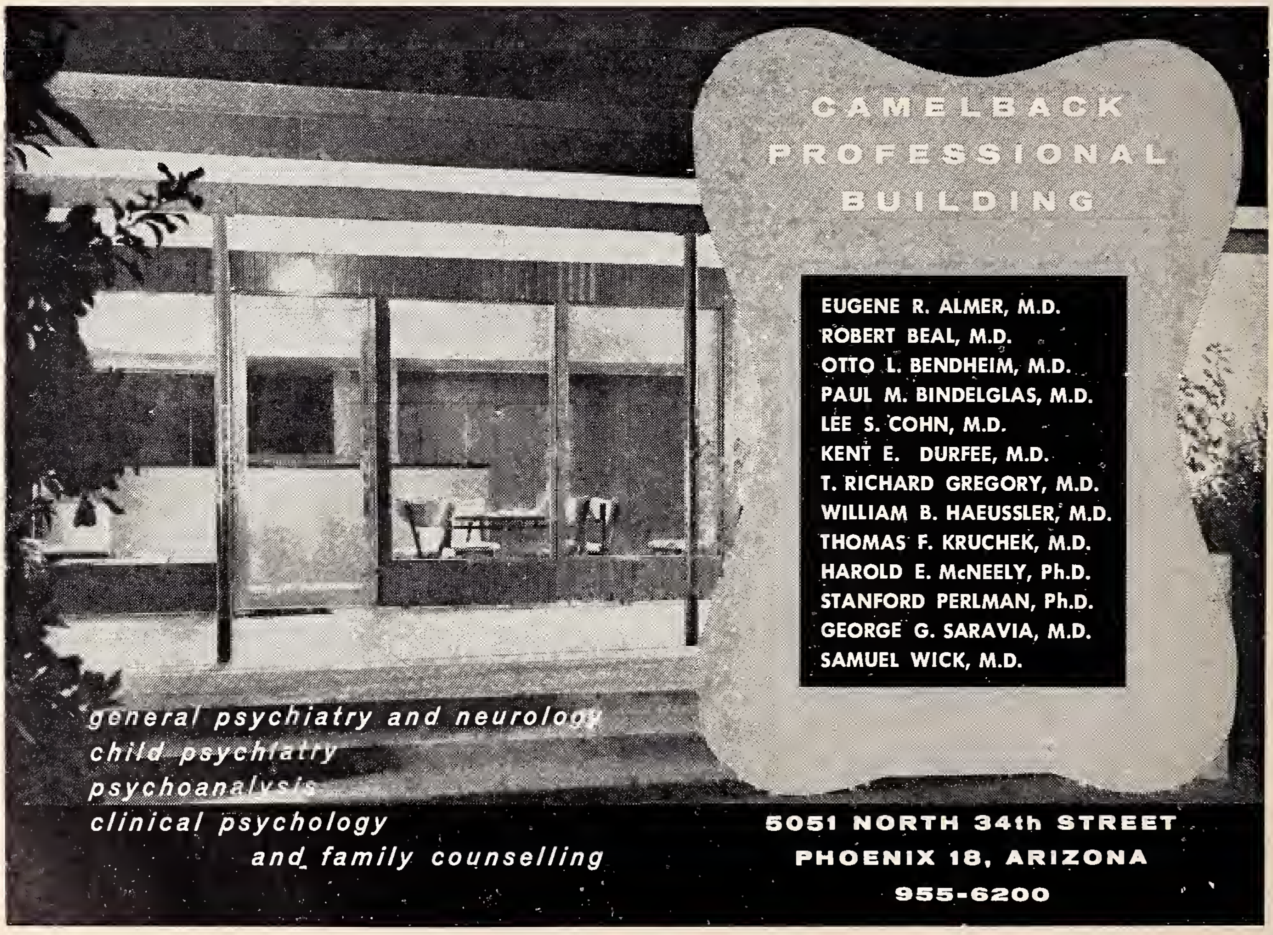

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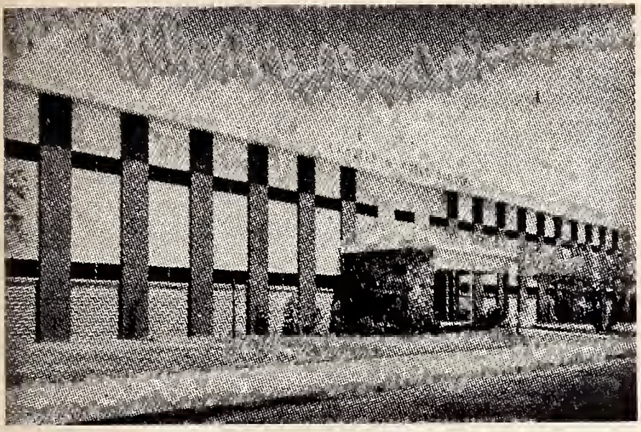

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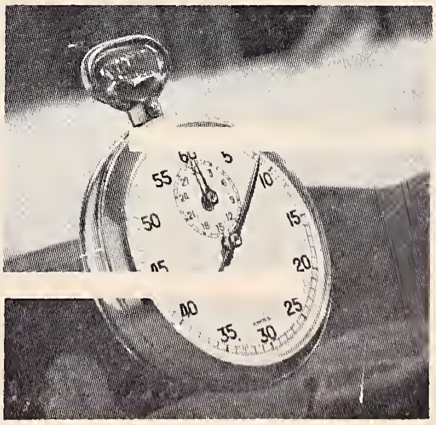

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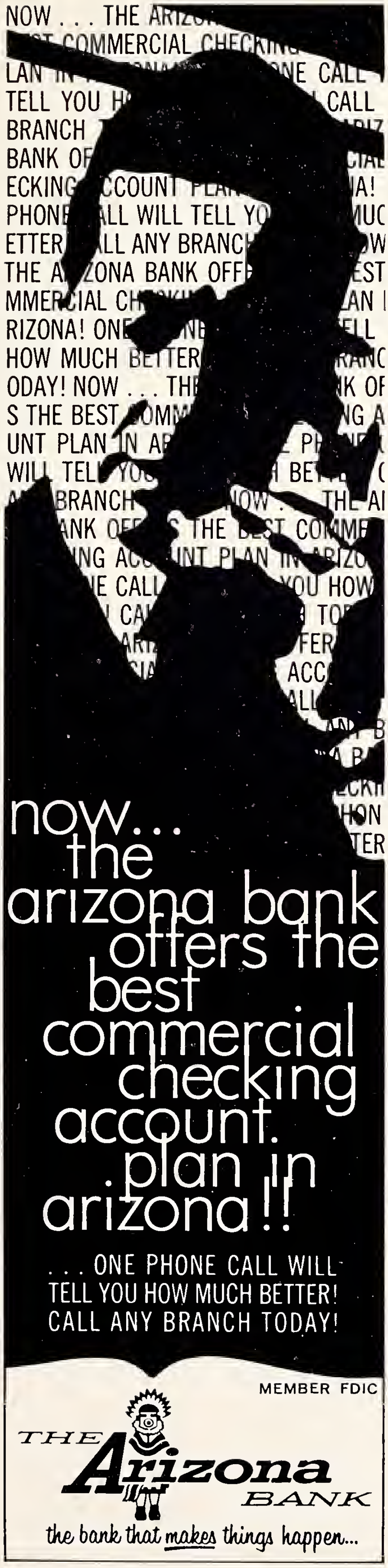

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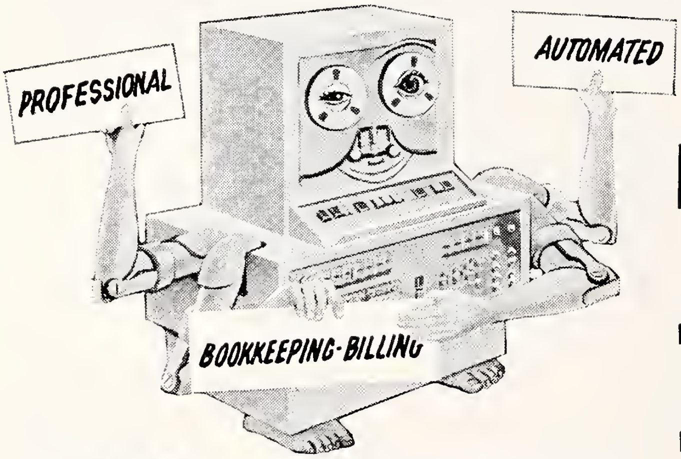

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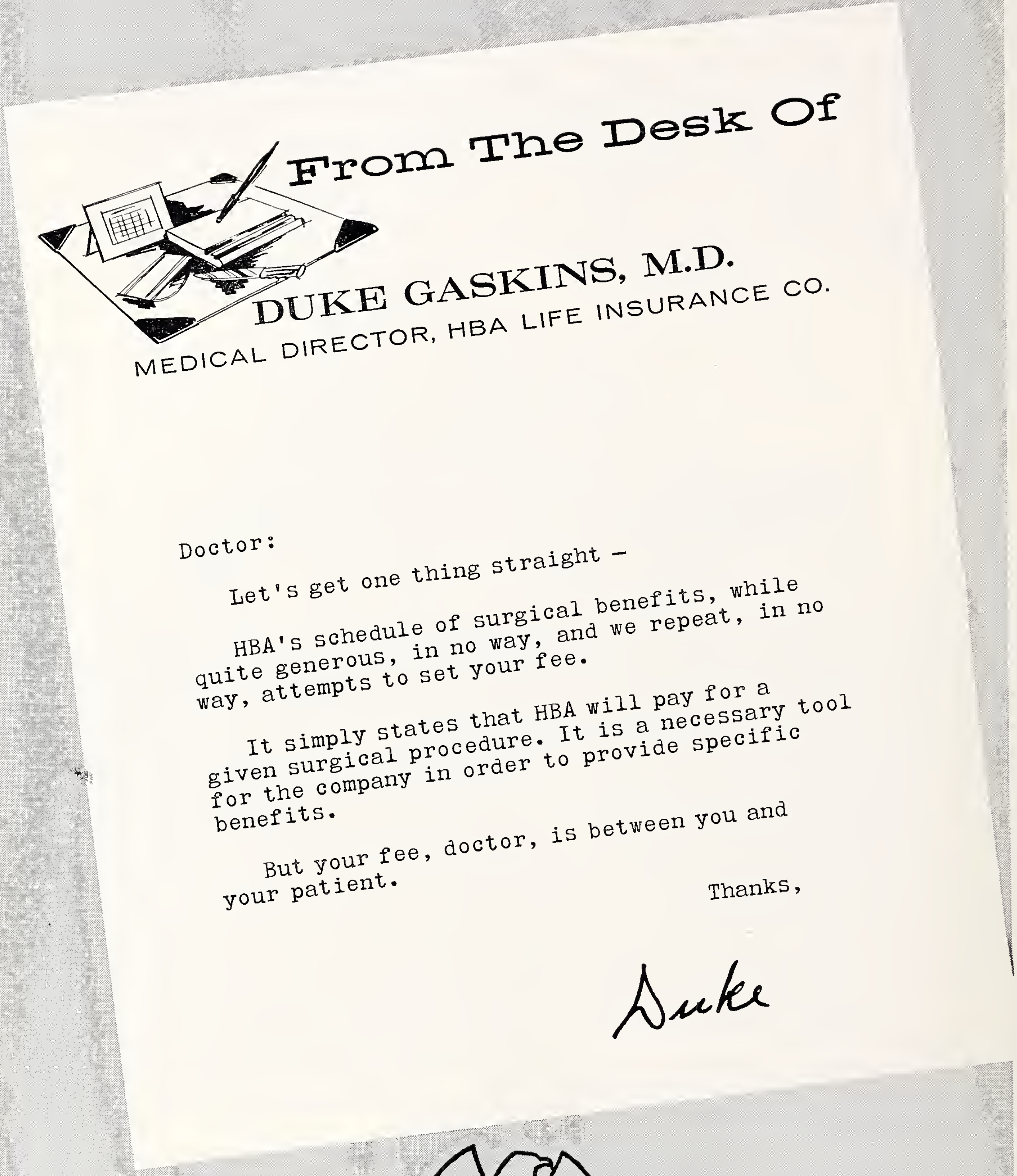

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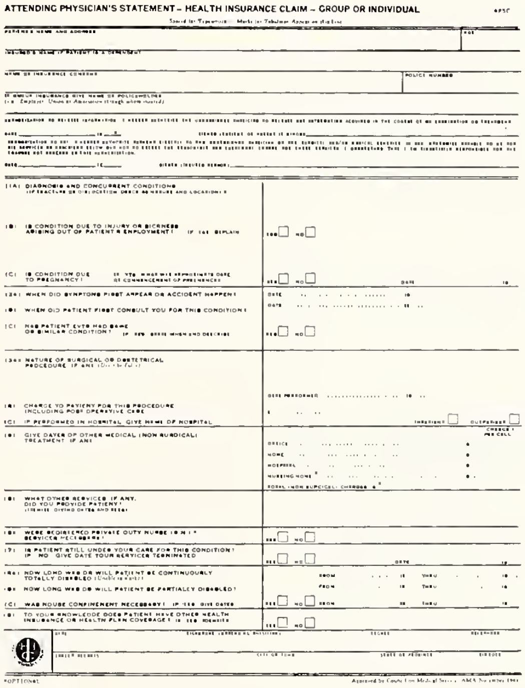

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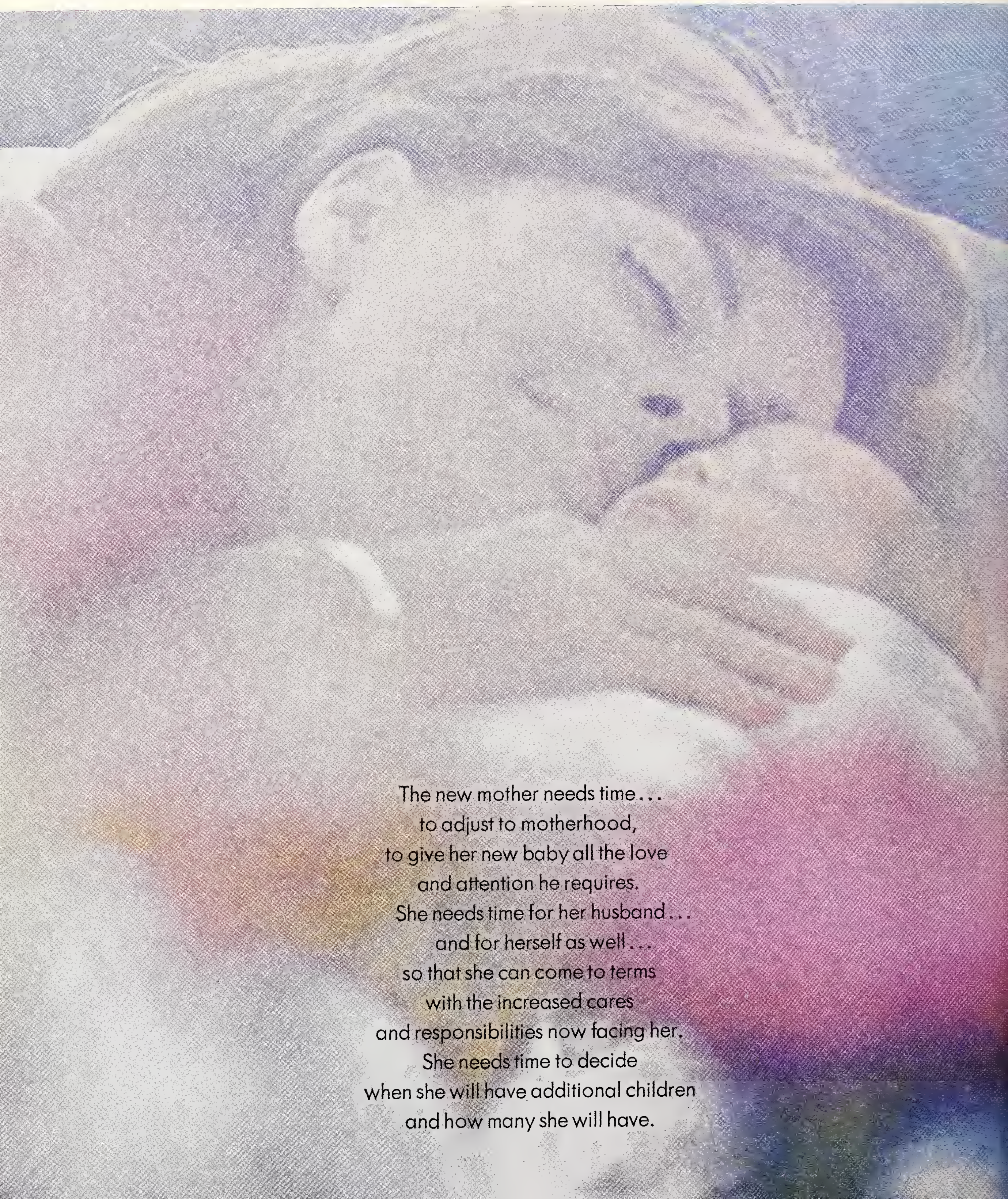

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The patient's tried aspirin.
What now?
100 TABLETS

There's a good chance your patient needs more than a non-prescription analgesic for pain relief. Especially after self-medication has failed.

Because continuing, increased pain and discomfort may in part be a reflection of anxiety, Equagesic is worthy of consideration. In a single, non-narcotic preparation, it helps relieve pain . . . *and* associated anxiety and tension.

Tablets

Equagesic®

(meprobamate and ethoheptazine citrate with aspirin) Wyeth

IN BRIEF

Contraindications: History of sensitivity or severe intolerance to aspirin, meprobamate or ethoheptazine citrate.

Warnings: USE IN PREGNANCY: Safety for use during pregnancy or lactation has not been established; therefore, it should be used in pregnant patients or women of child-bearing age only when the physician judges its use essential to the patient's welfare.

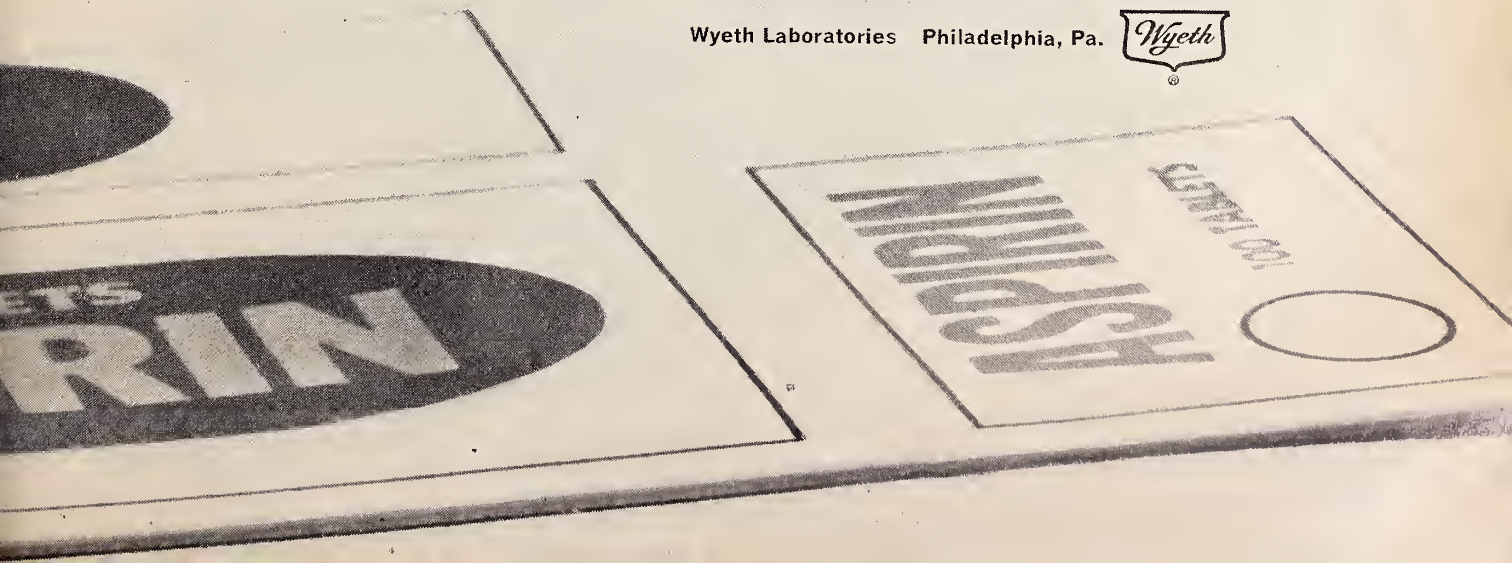
Precautions: Keep out of reach of children. Not recommended for patients 12 years old or less. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate in susceptible persons—as alcoholics, ex-addicts, severe psychoneurotics—has resulted in dependence or habituation. Withdraw gradually after prolonged excessive dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance, with resultant slowed reactions and impaired judgment and coordination. If drowsiness, ataxia or visual disturbances (impairment of accommodation and visual acuity) occur, reduce dose. If symptoms persist, patients should not operate machinery or drive. After meprobamate overdose, prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels, and hyperventilation are reported. Give cautiously and in small amounts to patients with suicidal tendencies. Treat attempted suicide (has resulted in coma, shock, vasomotor and respiratory collapse and anuria) with gastric lavage and appropriate symptomatic therapy (CNS stimulants and pressor amines as indicated). Two instances of accidental or intentional significant overdosage with ethoheptazine and aspirin have been reported. These were accompanied by CNS depression (drowsiness and lightheadedness) but resulted in uneventful recovery. On basis of pharmacologic data, CNS stimulation could be anticipated, with nausea, vomiting and salicylate intoxication (requires induced vomiting or gastric lavage, specific parenteral electrolyte therapy for ketoacidosis and dehydration, and observation for hypoprothrombinemic hemorrhage [usually requires whole blood transfusions]).

Adverse Reactions: Ethoheptazine and aspirin may cause nausea with or without vomiting and epigastric distress in a small percentage of patients. Dizziness is rare at recommended dosage. Meprobamate may cause drowsiness, ataxia and rarely allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses. Such patients may have had no previous contact with meprobamate and may or may not have an allergic history. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. If allergic reaction occurs, discontinue meprobamate; do not reinstitute. Severe reactions, observed very rarely, include fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. These cases should be treated symptomatically including, when indicated, such medication as epinephrine, antihistamine and possibly hydrocortisone. A few cases of leukopenia, usually transient, have been reported on continuous use. Rarely, aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported, almost always in presence of known toxic agents.

Overdosage: See precautions section for management of overdosage.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

Wyeth Laboratories **Philadelphia, Pa.** Wyeth®



"For all the happiness
mankind can gain
It is not in pleasure,
but in rest from pain."

John Dryden

Give your patients rest from pain

Empirin® Compound with Codeine Phosphate gr. 1/2, No. 3

Each tablet contains: Codeine Phosphate gr. ½ (Warning—May be habit forming), Phenacetin gr. 2½, Aspirin gr. 3½, Caffeine gr. ½.

B. W. & Co. narcotic products are Class "B", and as such are available on oral prescription, where State law permits.

Complete literature available on request from Professional Services Dept. PML.

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FREE MEDICAL CARE

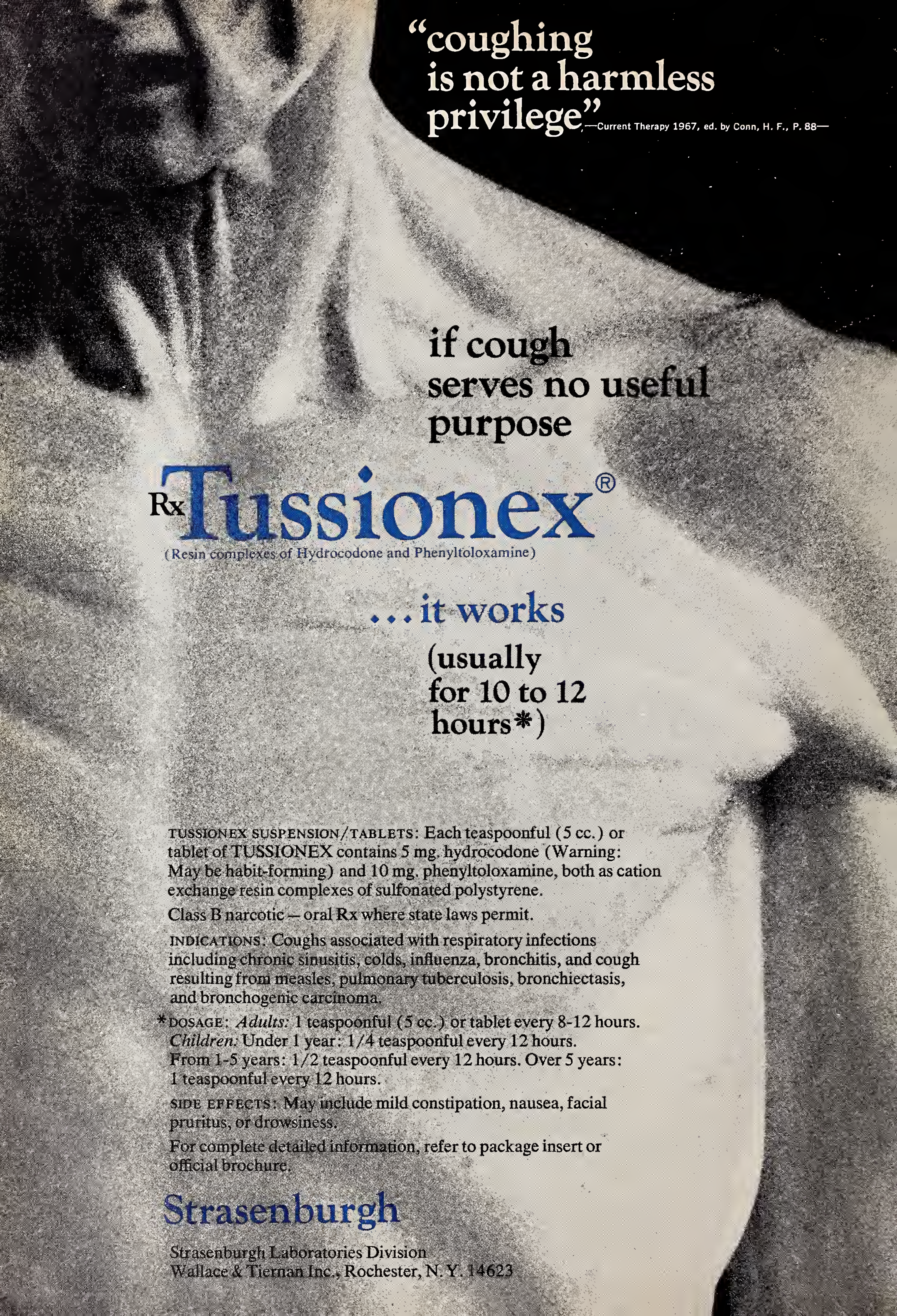
As national elections approach, we will hear more and more about both state and federal proposals for broad plans covering health needs of our citizens by providing "free" medical care.

In a recent bulletin of the Maricopa County Better Business Bureau an article appeared discussing misleading promotional schemes promising free vacations, which turn out to be less free than the advertising indicates. The article pointed out that as a result of deceptive advertising of free items, the Federal Trade Commission has issued a guide concerning the use of the word "free."

The guide suggests that when the word "free" is used in advertising, all of the terms, conditions and obligations associated with receipt of a free item of merchandise or service must be clearly and obviously stated. It discusses many unfair and misleading uses of the word "free," "given without charge," "bonus," and other phrases which convey the impression that an article or service is without cost. The purpose of the guide is "to encourage advertisers to voluntarily comply with the Federal Trade Commission Act which makes it illegal to employ any unfair methods of competition or unfair or deceptive acts or practices in commerce."

It might be well to have an additional guide for use by politicians promoting the vote attracting Utopian illusion of medical care available without cost to anyone. The only drawback is that it is unlikely that such a guide would be followed. If it were followed, however, the voter would no doubt be promised that although the plan might not be free, the cost would be covered by funds from the evergreen money tree on the banks of the Potomac, which has replaced the cherry blossoms as the symbol of Capitol elegance.

Robert F. Lorenzen, M.D.
Editor


"coughing
is not a harmless
privilege"—Current Therapy 1967, ed. by Conn, H. F., P. 88—
if cough
serves no useful
purpose
Rx Tussionex®
(Resin complexes of Hydrocodone and Phenyltoloxamine)
...it works
(usually
for 10 to 12
hours*)

TUSSIONEX SUSPENSION/TABLETS: Each teaspoonful (5 cc.) or tablet of TUSSIONEX contains 5 mg. hydrocodone (Warning: May be habit-forming) and 10 mg. phenyltoloxamine, both as cation exchange resin complexes of sulfonated polystyrene.

Class B narcotic—oral Rx where state laws permit.

INDICATIONS: Coughs associated with respiratory infections including chronic sinusitis, colds, influenza, bronchitis, and cough resulting from measles, pulmonary tuberculosis, bronchiectasis, and bronchogenic carcinoma.

*DOSAGE: *Adults:* 1 teaspoonful (5 cc.) or tablet every 8-12 hours. *Children:* Under 1 year: 1/4 teaspoonful every 12 hours. From 1-5 years: 1/2 teaspoonful every 12 hours. Over 5 years: 1 teaspoonful every 12 hours.

SIDE EFFECTS: May include mild constipation, nausea, facial pruritus, or drowsiness.

For complete detailed information, refer to package insert or official brochure.

Strasenburgh

Strasenburgh Laboratories Division
Wallace & Tiernan Inc., Rochester, N.Y. 14623

When diarrhea separates
a man from his job... DONNAGEL®

The concert was just underway,
When to the conductor's dismay
Cramps and diarrhea,
Did so quickly appear,
The maestro no longer could stay.

Because diarrhea with cramping, nausea, and painful straining can
e at the most inopportune time, it takes a comprehensive agent to treat the
diarrheal syndrome and help get the patient back on the job. That's why
nany physicians rely on Donnagel, especially during the fall and winter
ths when "flu" and viral gastroenteritis usually hit their peak.

Donnagel is much more than just a simple kaolin-pectin combination.
lso contains the belladonna alkaloids to calm GI hypermotility and help
ve the distressing discomforts which so often accompany diarrhea. Certainly
less expensive and more convenient than taking two medications. And the
ge is lower too. Available in the handy 4-oz. plastic bottle at pharmacies
ywhere on your prescription or recommendation.

Diarrhea and its Discomforts

Donnagel®

fluid ounce contains: Kaolin, 6 Gm.; Pectin, 142.8 mg.; Hyoscyamine sulfate,
7 mg.; Atropine sulfate, 0.0194 mg.; Hyoscine hydrobromide, 0.0065 mg.;
ım benzoate (preservative), 60 mg.; Alcohol, 3.8%.

ROBINS A. H. Robins Company, 1407 Cummings Drive, Richmond, Va. 23220

PHOTO BY VICT

CLEAR THE TRACT!

THERE'S A ROBITUSSIN FOR EVERY COUGHING NEED

All the Robitussins contain gylceryl guaiacolate, an outstanding expectorant agent that greatly increases the output of lower respiratory tract fluid. Increased RTF volume exerts a demulcent effect on the tracheobronchial mucosa, promotes ciliary action, and makes thick, inspissated mucus less viscid and easier to raise.

For coughs of colds and "flu"
ROBITUSSIN®
Each 5 cc. contains:
Glyceryl guaiacolate . . 100.0 mg.
Alcohol, 3.5%

Non-narcotic for 6-8 hr. cough control
ROBITUSSIN-DM®
Each 5 cc. contains:
Glyceryl guaiacolate . . 100.0 mg.
Dextromethorphan
hydrobromide . . . . 15.0 mg.
Alcohol, 1.4%

For unproductive allergic coughs
ROBITUSSIN A-C®
Each 5 cc. contains:
Glyceryl guaiacolate . . 100.0 mg.
Pheniramine maleate . . 7.5 mg.
Codeine phosphate . . . 10.0 mg.
(warning: may be habit forming)
Alcohol, 3.5%

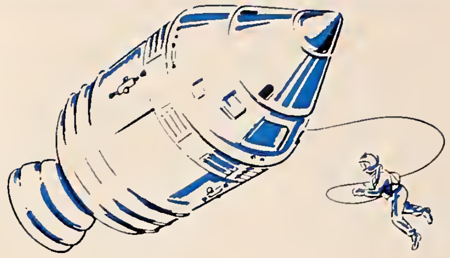
Clears sinuses and nasal stuffiness as it relieves cough
ROBITUSSIN-PE®
Each 5 cc. contains:
Glyceryl guaiacolate . . 100.0 mg.
Phenylephrine
hydrochloride. . . . . 10.0 mg.
Alcohol, 1.4%

Robitussin-DM in solid form for "coughs on the go"
COUGH CALMERS™
Each Cough Calmer contains:
Glyceryl guaiacolate . . 50.0 mg.
Dextromethorphan
hydrobromide . . . . 7.5 mg.

Use this handy guide to pick the right formulation for each coughing need

	Robitussin	Robitussin-DM	Robitussin A-C	Robitussin-PE	Cough Calmers
Expectorant	●	●	●	●	●
Demulcent	●	●	●	●	●
Cough Suppressant		●	●		●
Antihistamine			●		
Long-Acting (6-8 hours)		●			●
Nasal, Sinus Decongestant				●	
Non-narcotic	●	●		●	●

A·H·ROBINS A. H. Robins Company, Richmond, Va. 23220



Man in space, now fait accompli, re-emphasizes the importance of Uro-Phosphate therapy. Research into the effect of space travel on the astronaut reveals that weightlessness causes loss of bone calcium. As the bones are required to bear less and less of the weight of the body they lose calcium, increasing the calcium content of the urine. When physical activity is reduced, the acidity of the urine should be adjusted to keep increased calcium in solution . . . . a prophylaxis to prevent kidney or bladder calculi.

Uro-Phosphate®

NOW A SUGAR-COATED TABLET

Each tablet contains: METHENAMINE, *300 mg.;* SODIUM ACID PHOSPHATE, *500 mg.*

Uro-Phosphate gives comfort and protection when inactivity causes discomfort in the urinary function. It keeps calcium in solution, preventing calculi; it maintains clear, acid, sterile urine; it encourages complete voiding and lessens frequency when residual urine is present.

Uro-Phosphate contains sodium acid phosphate, a natural urinary acidifier. This component is fortified with methenamine which is inert until it reaches the acid urinary bladder. In this environment it releases a mild antiseptic keeping the urine sterile.

Uro-Phosphate is safe for continuous use. There are no contra-indications other than acidosis. It can be given in sufficient amount to keep the urine clear, acid and sterile. A heavy sugar coating protects its potency.

Dosage:

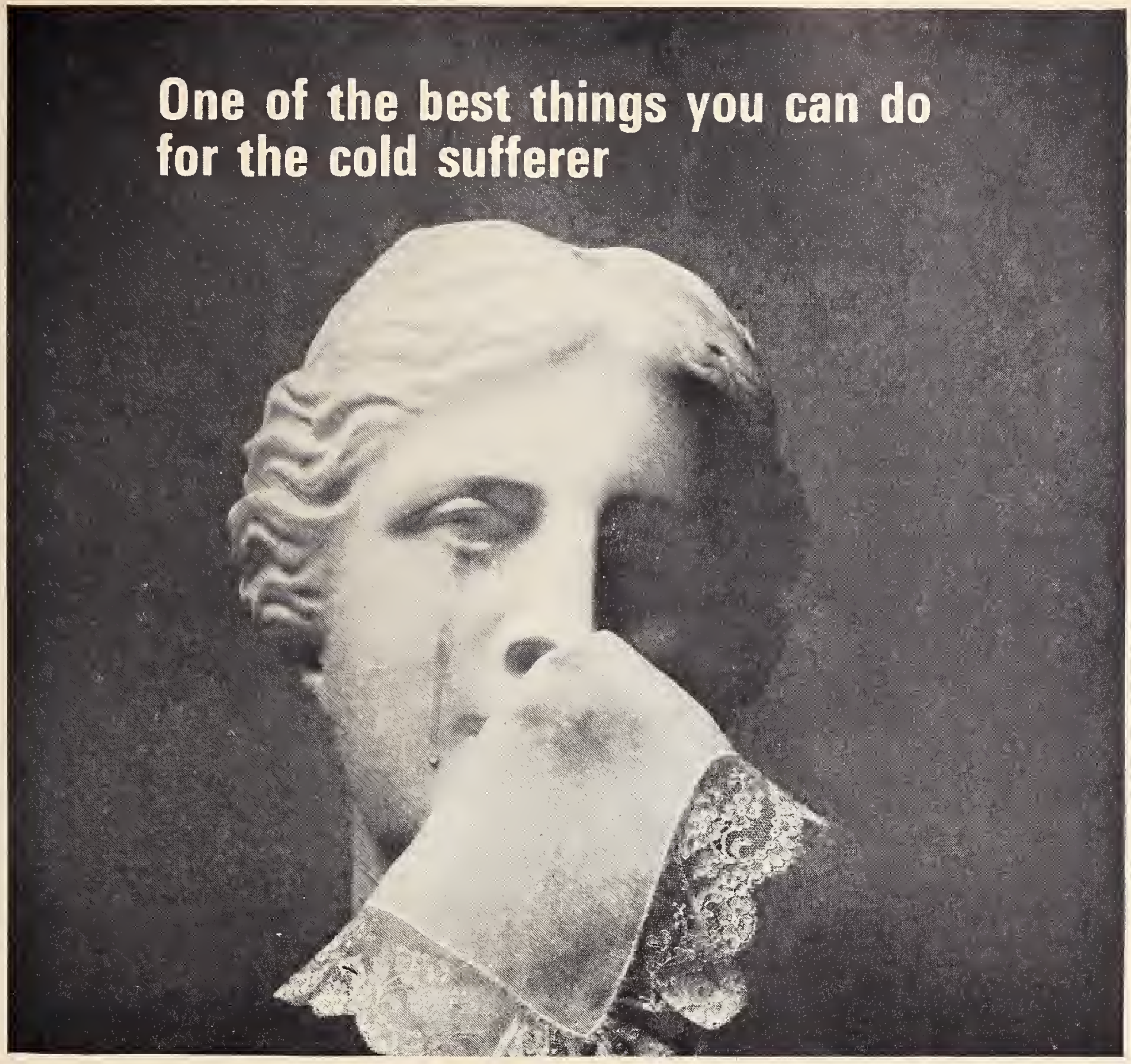
For protection of the inactive patient 1 or 2 tablets every 4 to 6 hours is usually sufficient to keep the urine clear, acid and sterile.

2 tablets on retiring will keep residual urine acid and sterile, contributing to comfort and rest.

A clinical supply will be sent to physicians and hospitals on request.

WILLIAM P. POYTHRESS & COMPANY, INC., RICHMOND, VIRGINIA 23217

Manufacturers of Ethical Pharmaceuticals


One of the best things you can do for the cold sufferer

Ornade® Spansule® brand of sustained release capsules

Trademark
Each capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate); 50 mg. of phenylpropanolamine hydrochloride; 2.5 mg. of isopropamide, as the iodide.

Prompt relief from nasal congestion and hypersecretion due to colds.

Before prescribing, see complete prescribing information in SK&F literature or *PDR*.
Contraindications: Glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloroduodenal or bladder neck obstruction.
Precautions: Use cautiously in the presence of hypertension, hyperthyroidism, coronary artery disease; warn vehicle or machine operators of possible drowsiness.
Usage In Pregnancy: Use in pregnancy, nursing mothers and women who might bear children only when potential benefits have been weighed against possible hazards.
Note: The iodine in isopropamide iodide may alter PBI test results and will suppress I^{131} uptake; discontinue 'Ornade' one week before these tests.
Adverse Reactions: Drowsiness; excessive dryness of nose, throat or mouth; nervousness; insomnia Other known possible adverse reactions of the individual ingredients: nausea, vomiting, diarrhea, rash, dizziness, fatigue, tightness of chest, abdominal pain, irritability, tachycardia, headache, incoordination, tremor, difficulty in urination. Thrombocytopenia, leukopenia and convulsions have been reported.
Supplied: Bottles of 50 capsules.

One capsule q12h for round-the-clock relief

SK&F **Smith Kline & French Laboratories**

lubadub lubadu

His heart tells him he's an invalid. You know he's not.

Photograph professionally posed.

badubdub lubadu

iety is expected in the cardiovascular patient. tle may even be desirable.

when anxiety is exaggerated . . . when it rferes with sleep . . . when it aggravates iovascular symptoms, your help may ieeded.

irally, you'll want to reassure the patient.

perhaps prescribe Equanil (meprobamate) djunctive therapy. It helps relieve anxiety tension specifically, yet gently.

ost 15 years' use has shown that Equanil sually well tolerated as well as effective. effects are generally limited to transient vsiness; serious, therapy-interrupting effects are rare.

Contraindications: History of sensitivity to meprobamate.

Important Precautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. (All tablets also available in REDIPAK® [strip pack], Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

Wyeth Laboratories Philadelphia, Pa.

Equanil®

(meprobamate) Wyeth®

Pertofrane® desipramine hydrochloride

Indication: Mental depression.

Contraindications: Do not use MAO inhibitors concomitantly or within 2 weeks of the use of this drug. Hyperpyretic crises or severe convulsive seizures may occur with such combinations; potentiation of adverse reactions can be serious or even fatal.

When substituting Pertofrane in patients receiving an MAO inhibitor, allow an interval of at least 14 days. Initial dosage in such patients should be low and increases should be gradual and cautiously prescribed.

The drug is contraindicated following recent myocardial infarction and in patients with a known hypersensitivity to tricyclic antidepressants.

Warning: Activation of psychosis may occasionally be observed in schizophrenic patients. Due to atropine-like effects and sympathomimetic potentiation, use only with the greatest care in patients with narrow-angle glaucoma or urethral or ureteral spasm.

Do not use in patients with the following conditions unless the need outweighs the risk: severe coronary heart disease with EKG abnormalities, progressive heart failure, angina pectoris, paroxysmal tachycardia and active seizure disorder (may lower seizure threshold).

Desipramine and the parent compound, imipramine, have been shown to block the action of guanethidine and related adrenergic neuron-blocking agents.

Hypertensive episodes have been observed during surgery.

The concurrent use of other central nervous system drugs or alcohol may potentiate adverse effects. Since many such drugs may be used during surgery, desipramine should be discontinued prior to elective procedures.

Caution patients on the possibility of impaired ability to operate a motor vehicle or dangerous machinery.

Do not use in women who are or may become pregnant unless the clinical situation warrants the potential risk, and do not use in patients under 12 years of age.

Because of increased sensitivity to the drug, use lower than normal dosage in adolescent and geriatric patients.

Precautions: Potentially suicidal patients require careful supervision and protective measures during therapy. Discontinuation of the drug may be necessary in the presence of increased agitation and anxiety shifting to hypomanic or manic excitement.

Atropine-like effects may be more pronounced (e.g. paralytic ileus) in susceptible patients and in those receiving anticholinergic drugs (including antiparkinsonism agents).

Prescribe cautiously in hyperthyroid patients and in those receiving thyroid medications; transient cardiac arrhythmias have occurred in rare instances.

Periodic blood and liver studies should supplement careful clinical observations in all patients undergoing extended courses of therapy.

Adverse Reactions: The following have been reported: *Nervous System:* dizziness, drowsiness, insomnia, headache, disturbed visual accommodation, tremor, unsteadiness, tinnitus, paresthesias, changes in EEG patterns, epileptiform seizures, mild extrapyramidal activity, falling and neuromuscular incoordination. A confusional state (with such symptoms as hallucinations and disorientation), particularly in older patients and at higher dosage, may require discontinuation of the drug. *Gastrointestinal Tract:* anorexia, dryness of the mouth, nausea, epigastric distress, constipation and diarrhea. *Skin:* skin rashes (including photosensitization), perspiration and flushing sensations. *Liver:* rare cases of transient jaundice (apparently of an obstructive nature) and liver damage. If jaundice or abnormalities in liver function tests occur, discontinue the drug and investigate. *Blood Elements:* bone-marrow depression, agranulocytosis, thrombocytopenia and purpura. If these occur, discontinue the drug. Transient eosinophilia has been observed. *Cardiovascular System:* orthostatic hypotension and tachycardia. Carefully supervise patients requiring concomitant vasodilating therapy, particularly during initial phases. *Genitourinary System:* urinary frequency or retention and impotence. *Endocrine System:* occasional hormonal effects, including gynecomastia, galactorrhea and breast enlargement, and decreased libido and estrogenic effect. *Sensitivity:* urticaria and rare instances of drug fever and cross-sensitivity with imipramine.

Dosage: All patients except geriatric and adolescent: 50 mg. t.i.d. (150 mg daily). Dosage may be increased up to 200 mg. daily. Geriatric and adolescent patients should usually be started with lower dosage (25 to 50 mg. daily) and may not tolerate higher doses. Dosage may be increased up to 100 mg. daily.

Lower maintenance dosages should be continued for at least 2 months after obtaining a satisfactory response.

Mild anxiety and agitation which may accompany depression usually remit as the depression responds. Occasionally, however, a sedative or tranquilizer may be indicated.

Availability: Maroon and pink capsules of 50 mg. in bottles of 100, pink capsules of 25 mg. in bottles of 100 and 1000.
(B)46-530-G

For complete details, please see the full prescribing information.

Coming out of a depression.

And it can often begin to happen in 3 to 5 days with an antidepressant like Pertofrane. There's a lifting of depressed mood . . . a restoration of psychomotor activity. Patients usually begin to cope, work, maybe play, even enjoy.

It's not all beautiful. Sometimes there are side effects. And not everybody can take the drug. It may even be a slow process. But along with the care and comfort you give depressed patients, consider Pertofrane. Then consider the response

Please read the prescribing information for full details on contraindications, warnings, precautions, adverse reactions and dosage. It's summarized on the left.

Pertofrane®

desipramine hydrochloride

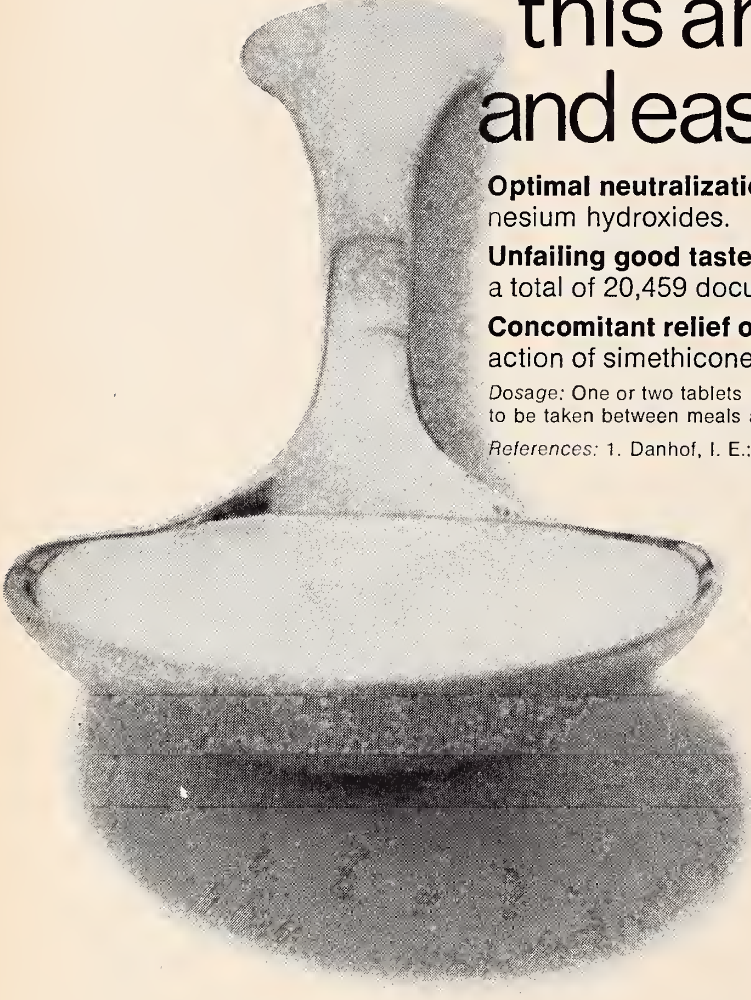
New 50-mg. capsules now available.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
Ardsley, New York 10502

It's beautiful!

the thousandth teaspoonful

Peptic ulcer patients find the thousandth dose of this antacid as effective and easy-to-take as the first!



Optimal neutralization—provided by the combination of aluminum and magnesium hydroxides.

Unfailing good taste—confirmed by 87.5% of 104 patients in one study, after a total of 20,459 documented days on Mylanta Liquid or tablets.[1]

Concomitant relief of G. I. gas distress—provided by the proven antiflatulent action of simethicone.[2]

Dosage: One or two tablets (well chewed or allowed to dissolve in the mouth); one or two teaspoonfuls to be taken between meals and at bedtime, or as directed by physician.

References: 1. Danhof, I. E.: Report on file. 2. Hoon, J. R.: Arch. Surg. *93*:467 (Sept.) 1966.

Mylanta®

LIQUID/TABLETS

aluminum and magnesium hydroxides *plus* simethicone

Stuart Division/ATLAS CHEMICAL INDUSTRIES, INC./Pasadena, Calif. 91109

'icture of
:orticollis

treated with
Parafon Forte® TABLETS

Paraflex® (chlorzoxazone)* 250 mg.
Tylenol® (acetaminophen) 300 mg.

'arafon Forte tablets help to relieve pain, estore mobility... stop pain-spasm feedback

y providing:

nonsalicylate analgesic equal to aspirin for the relief pain,[1,2] yet unlikely to produce the irritation to the ıstric mucosa so often associated with salicylate erapy[3]

ıd a skeletal muscle relaxant shown to have up to a hour span of action[4]...to retain effectiveness even continued administration[4]...but not likely to have e central effects of tranquilizing compounds.[5]

rescribe PARAFON FORTE for effective spasmolysis ıd analgesia in sprains, strains, myalgias, low back ıin, bursitis and other musculoskeletal disorders. ıur patients will appreciate the restored comfort ıd freedom of movement it usually provides.

Contraindications: Sensitivity to either component. ***Precautions:*** Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped. ***Adverse Reactions:*** Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, *Paraflex* (chlorzoxazone) may possibly have been associated with gastrointestinal bleeding. While *Paraflex* (chlorzoxazone) and chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately eighteen patients, it was not possible to state that the dysfunction was or was not drug induced. ***Usual Adult Dosage:*** Two tablets q.i.d. ***Supplied:*** Scored, light green tablets, imprinted "McNEIL"—bottles of 100.

References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth, J. L. A., *et al.*: Gastroenterology *44*:146, 1963. 4. Berman, H. H., *et al.*: Dis. Nerv Syst. *25*:430, 1964. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

McNEIL

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*U.S. PATENT NO. 2,895,877

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Inner Sites...

In Cystitis...Azo Gantanol® focuses analgesic-antibacterial activity where it counts

Blood and urine: therapeutic antibacterial levels within 2 hours for up to 12 hours

Gantanol (sulfamethoxazole) produces prompt and prolonged therapeutic levels, in both blood and urine, with convenient *b.i.d.* dosage. Clinical response is usually obtained within 24 to 48 hours. The wide antibacterial spectrum of Gantanol includes *E. coli* and a variety of other susceptible gram-negative and gram-positive pathogens in urinary tract infections.

The mucosa: specific analgesia usually within 30 minutes

Azo (phenazopyridine HCl) effects specific mucosal analgesia, relieving the dysuria, discomfort and burning which are virtually always a part of acute urinary tract infections.

Interstitial fluids: ready diffusion of antibacterial

Gantanol (sulfamethoxazole) is readily diffused into interstitial fluids to provide efficient antibacterial activity at foci of infection. This distribution, plus continuous antibacterial levels in blood and urine, has afforded effectiveness in the majority of infections in which it has been used.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Urinary tract infections with associated pain or discomfort when due to susceptible organisms; prophylactically in urologic surgery, catheterization and instrumentation.

Contraindicated in sulfonamide-sensitive patients, pregnant females at term, premature infants, newborn infants during the first three months of life, glomerular nephritis, severe hepatitis, uremia and pyelonephritis of pregnancy with gastrointestinal disturbances.

Warnings: Use only after critical appraisal in patients with liver damage, renal damage, urinary obstruction or blood dyscrasias. If toxic or hypersensitivity reactions or blood dyscrasias occur, discontinue therapy. In closely intermittent or prolonged therapy, blood counts and liver and kidney function tests should be performed.

Precautions: Observe usual sulfonamide therapy precautions including maintenance of an adequate fluid intake. Use with caution in patients with histories of allergies and/or asthma. Patients with impaired renal function should be followed closely since renal impairment may cause excessive drug accumulation. Occasional failures may occur due to resistant microorganisms. Not effective in virus and rickettsial infections.

Adverse Reactions: Headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, Stevens-Johnson syndrome, injection of the conjunctiva and sclera, petechiae, purpura, hematuria or crystalluria may occur, in which case the dosage should be decreased or the drug withdrawn.

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Azo Gantanol®

(Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.)

No place for beginners

Terramycin®
(oxytetracycline)

An infection of rapid onset requiring prompt attention. Teenage girl with chills, fever, abdominal pain, backache and nausea. Frequent and urgent urination with burning. On examination—tenderness over kidney. Blood count and urinalysis confirm the diagnosis: acute pyelonephritis. Treatment is initiated with Terramycin. Within a few days of follow-up therapy, the patient is markedly improved. The pretreatment urine culture shows a strain of *E. coli* highly susceptible to Terramycin.

Experience has shown that Terramycin offers special advantages in treating urinary tract infections when strains of causative bacteria are susceptible. Broad-spectrum coverage unaffected by penicillinase. Effective tissue levels to help reach foci of infection in renal parenchyma. High urine levels—excreted by kidney in *active* form.

With Terramycin, you have the assurance that comes with choosing an agent physicians have depended on for over 18 years. In difficult as well as routine cases, when tests reveal susceptible organisms, consider Terramycin. One of the world's most widely used broad-spectrums.

Contraindicated: In individuals hypersensitive to oxytetracycline.

Warnings: Reduce usual oral dosage and consider antibiotic serum level determinations in patients with impaired renal function.

Use of oxytetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of developing teeth. This effect occurs mostly during long-term use of the drug, but it has also been observed in usual short-treatment courses.

During treatment with tetracyclines, individuals susceptible to photodynamic reactions should avoid direct sunlight; if such reactions occur, discontinue therapy.

Note: With oxytetracycline, phototoxicity is unknown and photoallergy very rare.

Precautions: Use of broad-spectrum antibiotics occasionally may result in overgrowth of nonsusceptible organisms. Where such infections occur, discontinue oxytetracycline and institute specific therapy. Increased intracranial pressure in infants is a possibility. Symptoms disappear upon discontinuation of therapy.

Adverse Reactions: Nausea, diarrhea, glossitis, stomatitis, proctitis, vaginitis and dermatitis, as well as reactions of an allergic nature, may occur but are rare.

Supply:* Terramycin Capsules: oxytetracycline HCl, 250 mg. and 125 mg. Terramycin Syrup: calcium oxytetracycline, 125 mg. per 5 cc. Terramycin Pediatric Drops: calcium oxytetracycline, 100 mg. per cc.

*All potencies listed are in terms of the standard, oxytetracycline.

More detailed professional information available on request.

Terramycin®
(oxytetracycline)

Pfizer LABORATORIES DIVISION
New York, N.Y. 10017

Appearances may be deceiving

It may be tetracycline

but it's not ACHROMYCIN® V
Tetracycline HCl

unless it bears this signature.

250 mg. and 100 mg. capsules

Contraindications: Hypersensitivity to tetracyclines.
Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.
Precautions: Nonsusceptible organisms may overgrow; treat superinfection appropriately. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Side Effects: Gastrointestinal—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

Upon adverse reaction, stop medication and treat appropriately.

Lederle

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530-9

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ArMA Reports

THE MINUTES APPEARING IN THIS SECTION HAVE BEEN EDITED TO CONSERVE SPACE. A COMPLETE COPY OF THE MINUTES OF ANY MEETING WILL BE MAILED TO ANY MEMBER REQUESTING THEM.

PROFESSIONAL COMMITTEE

Meeting of the Professional Committee of The Arizona Medical Association, Inc., held Saturday, September 27, 1969, in the French Quarter of the Safari Hotel, 4611 North Scottsdale Road, Scottsdale, Arizona, convened at 1:05 P.M., Albert G. Wagner, M.D., Chairman, presiding.

MINUTE

Approved Minute of the Professional Committee meeting held February 15, 1969.

FINANCE

Reported, as of August 31, 1969, expenditures totalling $1,295.76; further, that the Board of Directors in meeting held September 14, 1969, following review of the current Association financial situation, determined it necessary among others, to reduce by $5,000.00, the 1969 budget appropriation allotted for activities of the Professional Committee to $2,5000.00. The Chairman of the Board assured this committee that if there is dire need for further expenditure beyond the allotted amount, that this would certainly be very carefully considered. RECEIVED.

SECTION REPORTS

Aging and General Medicine

DIABETES DETECTION: Mr. Joseph Nicholls, President-Elect of the Pharmaceutical Association, contacted the Association suggesting the co-sponsorship of a diabetes detection drive for the State of Arizona during National Diabetes Week in November of this year. Dr. Kohl wrote he has carefully considered the suggestion and in view of our experience several years ago with a statewide diabetes detection drive, he would strongly recommend that the Arizona Medical Association not attempt to participate in such a program again this year. He further stated: as you will recall, our efforts several years ago were fraught with problems and brought much criticism from a number of our members. While we did discover a few previously undetected diabetics in the population tested, I am convinced that the small return was certainly not worth the tremendous effort and expense inherent in the program. We could certainly assist the pharmacists if they decide to go ahead by publicizing their program to our membership and at the same time again encouraging Arizona physicians to be alert for latent diabetes mellitus in their patients. RECEIVED FOR INFORMATION.

HOSPITAL EMERGENCY ROOM-PHYSICIAN RESPONSIBILITY: Robert E. Westfall, M.D., Secretary, Coconino County Medical Society, writes in the matter of physician responsibility in the hospital emergency room. The physicians of that society request guidelines from the state Association as to emergency room coverage for "call patients," and they desire to have it clarified as to whether or not there are any legal reasons why a physician cannot request a patient to be sent from the emergency room to his office provided the situation is not critical. Dr. Kohl wrote: this is, as you know, a very difficult subject and currently a number of hospitals are providing full time emergency room coverage. I believe this should be discussed at the Professional Committee meeting and perhaps a legal opinion obtained from counsel. It certainly would be helpful if our association could come up with a series of guidelines concerning care of the emergency room patient.

It was regularly moved and carried that this matter be referred to the Board of Directors requesting legal counsel in this regard.

TB SKIN TESTS: RECEIVED FOR INFORMATION, action of the Board of Directors in meeting held March 9, 1969, in response to certain questions raised by the Arizona State Nurses' Association over action of the State Board of Education authorizing school nurses to administer TB skin tests to certificated personnel.

CANCER REGISTRIES AND SCREENING: Dr. Kohl further wrote: several communications have also been received concerning cancer registries and cancer screening. In the past we have discussed this at great length and our decisions are a matter of previous record. I think this need not be considered any further. RECEIVED FOR INFORMATION.

GERIATRICS: Concerning the letter from the Pennsylvania Medical Society, Commission on Geriatrics, Dr. Kohl advised by letter: I did not complete and return the questionnaire. Inasmuch as we do not really have an active program in the field of geriatrics I was unable to provide any of the information requested. RECEIVED FOR INFORMATION.

SNAKEBITE TREATMENT: William J. Fielder, Ph.D., Child Study and Consultation, School Psychological Services, seeks an official statement from the Association concerning advisable procedures and most suitable emergency treatment which laymen should employ in the case of snakebite. Dr. Kohl wrote: I believe that the standard and most beneficial treatment has been well outlined in numerous publications. Immediate application of a tourniquet above the site of the bite followed by incision at the point of entry and suction is about all that can and need be done until the victim can receive specific antivenin at a hospital or physician's office. Persons who are in repeated contact with venomous snakes usually have antivenin in their possession for immediate use. If the Association wishes to make an "official statement," I think it might be well to seek the advice of a herpetologist. RECEIVED FOR INFORMATION.

Allied Medical Groups

VOLUNTARY HEALTH AGENCIES ACTIVITY: No report.

ARIZONA STATE HOSPITAL EMPLOYMENT OF ASTEOPATHS: Willis H. Bower, M.D., Director, Arizona State Hospital, seeks the attitude, policy, and/or action of this Association as to the employment of osteopathic physicians by that institution and admission to membership on its medical staff. The Board of Directors of this Association in meeting held July 27, 1969, having previously referred the matter to this Committee for study and recommendation, and further, while awaiting its report, directed that a letter be forwarded to Dr.

Bower advising him that it would approve the hiring of well-qualified, fully licensed physicians for positions in the state.

It was regularly moved and carried that doctors of osteopathy be accepted as physicians at the Arizona State Hospital if they meet the usual qualifications.

SOCIETY MEMBERSHIP OSTEOPATHS: RECEIVED FOR INFORMATION, letter of the co-chairman of the Parliamentary and Bylaws Committee of Maricopa County Medical Society, addressed to the AMA Committee on Osteopathy, seeking certain information regarding acceptance of osteopaths to membership. Dr. Helme requested to write AMA in the matter.

MEDICAL-LEGAL GRIEVANCE: As regards the relationship between the medical and legal professions in the matter of medical-legal grievances, Dr. Helme reported the state organization has been very inactive while on the local level, Maricopa County Medical Society has been very active in the areas of doctors' testimony, reports, etc. AMA urges improved liaison. RECEIVED FOR INFORMATION.

ArMA-ASNA Liaison

MEMBERSHIP: ArMA Liaison: Drs. Boyden L. Crouch (Phoenix), Arthur V. Dudley, Jr. (Tucson), Richard O. Flynn (Tempe), William G. Payne (Tempe), Chairman, and Joseph C. White, Jr. (Phoenix); ASNA Liaison: Hazel Bennett, R.N. (Phoenix), Dorothy Corona, R.N. (Tempe), Roosamond Gabrielson, R.N. (Phoenix), Sister John Richard (has name change) of Tucson, and Betty Spaulding, R.N. (Tucson).

ACTIVITY: This joint liaison committee has been active, meetings have been held January 19, 1969, March 22, 1969, and May 24, 1969.

AMA CONFERENCE ON NURSING: Dr. Payne reported that he had attended the Second National Conference on Nursing held in Chicago, April 11 and 12, 1969. A detailed copy of report is on file. Copies are available and will be distributed to members of the joint liaison committees. It is anticipated representatives from the American Hospital Association will be invited to attend the Third National Conference. RECEIVED FOR INFORMATION.

WORKSHOP-PATIENT CARE MESA-VELDA ROSE: Arrangements have been completed for the scheduled Workshop to be held at Velda Rose, Mesa, October 10 and 11, 1969. This meeting is sponsored by the Arizona Medical Association and the Arizona State Nurses' Association. The theme: "Improved Patient Care," how we can better take care of patients. Its purpose is: (1) to promote communication between physicians and nurses; (2) to promote feed-back from all areas of state and areas of practice; and (3) to promote awareness of the social changes. The meeting will open with a social hour and buffet Friday, October 10, 1969. The welcome and keynote addresses will be by Eleanor C. Lambertsen, R.N., Education Director, Division of Health Services and Education, Teachers College, Columbia University, New York, and Barbara Bates, M.D., Associate Professor of Medicine, University of Rochester Medical Center, Rochester, New York. Workshops will be conducted Saturday following. RECEIVED FOR INFORMATION.

Athletic Medicine

In the absence of the Chairman, Dr. Toll, no report submitted.

Disaster Medicine

BURN AND TRAUMA UNITS – ARIZONA: In the absence of Dr. Baker, Dr. Wagner read his written report. This Section held its annual meeting April last. Over 35 people were in attendance. The subject related to need for one or more Burn and Trauma Units in Arizona. Definite need was indicated for the future development of adequate emergency care in the state. A feasibility study is being continued by the Comprehensive Health Planning Council Committee, a sum of $20,000.-00 being made available by that body, September 26, 1969, for use by the consulting company to be employed for this study. RECEIVED FOR INFORMATION.

EMERGENCY CARE: Compliments were extended to the Section on Emergency Care and in particular to Dr. Schaller, its chairman, also Sister Mary Ralph, for its fine work and leadership. RECEIVED FOR INFORMATION.

BACTERIOLOGICAL AND CHEMICAL WARFARE: The Professional Committee is asked to go on record in support of bacteriological and chemical warfare research being conducted at Ft. McLelland, Alabama, as a major aid to the defense of our country. NO ACTION.

Emergency Care

EMERGENCY MEDICAL SERVICES – NADEC: The Regional Public Health Services Office, Division of Emergency Health Service – USPHS, suggests development of a forum or training program of council on emergency medical services on an individual state basis. It is possible this could be financed using limited Federal funds. Dr. Schaller reported the development of the NADEC council, a combined program for northern Arizona counties to update their emergency services, their ambulance services and possibly obtain some helicopters. This might be a project appropriately to be included in the program suggested by the public health services.

It was regularly moved and carried that we forward this on to Victor E. Rothe, Research Association, Arizona State University, who is writing the proposal, to possibly include a phase of this in his program.

AMES PROGRAM: The AMES Program appears to be operating pretty well since its inception May 31 of this year. The Federal Department of Transportation recently approved an extension of four months which will carry the program into 1970. Following conclusion of this program it is projected that it will be taken over by the Department of Highway Patrol or some other state agency. Approximately 95 Medivac missions have been flown, a portion of which include the transfer of patients from one hospital to another. (90% were evacuation missions.) Statistical data will be prepared at the end of the mission. It is apparent for varied reasons that the helicoptor is not the best vehicle to use at all times for the evacuation of injured persons. It has, of course, advantages and disadvantages, particularly vibration and noise in the latter instance.

Another aspect of the AMES report is the Simbol Rating System. It is a two part rating system to get a numerical estimate of (1) the severity of the condition of the patient, and (2) a projected rate of deterioration of the patient.

It was regularly moved and carried that this Simbol Rating System be approved by this Professional Committee with the recommendation to the Board of Directors that we search out ways to implement its use by all citizens and teaching in all first aid courses.

DRIVERS LICENSING: Dr. Schaller stated that he is a member of the Drivers Licensing Advisory Committee to the Highway Safety Department. He will attend a hearing Monday before the Transportation Committee of the Senate which body is considering a bill to become an Enabling Act to give this committee authority to set standards and procedures and history taking methods for examining driver license applicants — give authority to take a history from a patient in the form of a simple physical appraisal of the patient by the non-physician, non-nurse driver license examiner. RECEIVED FOR INFORMATION.

RURAL HEALTH CONFERENCE: Dr. Schaller reported that he had attended the meeting of the AMA Council on Rural Health held in Chicago, September fifth, as a representative of a local hospital, stating he was enlightened and disappointed. Reviewing the membership composite of the Council on Rural Health, he noted that it had no representation of any group representing medical education or the hospital association, or any specialty groups in the country. In his opinion, the Council is trying to do something about rural health and it appears to him that they have a group of people that have the least idea of the best way to go about increasing the health care in rural areas. He told them so at this meeting. He presented the AMES Program being conducted here in Arizona and in all probability it will be made a part of the program at its next meeting to be held in Milwaukee. RECEIVED FOR INFORMATION.

CARDIAC ARREST: RECEIVED FOR INFORMATION, resolution adopted by the Board of Directors of this Association in meeting held March 9, 1969, pertaining to cardiac arrest.

Industrial Health

ACTIVITIES: Dr. Ryan expressed his concern regarding the fragmentation and duplication of activity and scope of operation within the Section on Industrial Health of the Professional Committee, the Medical Economics Committee and the Industrial Relations Committee. It is his feeling that the duties of each should be more specifically outlined with possible consolidation into one functional committee. Discussion ensued. Suggestions included preparaton of job description or outline by the Board of Directors with the assistance of staff; that Dr. Ryan get in touch with the Chairman of the Medical Economics Committee, Dr. Harvey G. Brown, to see if they couldn't work this out and establish a definite line of involvement; and that Staff confer with AMA to ascertain its scope of operation in these areas and report to Dr. Ryan.

CONGRESS ON OCCUPATIONAL HEALTH: Dr. Ryan stated he had included in his written report a detailed accounting of 29th Annual AMA Congress on Occupational Health held in St. Louis, September 15 and 16, 1969, which he attended. Generally, discussion entailed Airport Medical Care, Rural Care, and Occupational Medicine. RECEIVED FOR INFORMATION.

INDUSTRIAL HEALTH CONFERENCE: The 13th Annual Western Industrial Health Conference will be held in San Francisco, October 17 and 18, 1969. RECEIVED FOR INFORMATION.

Medical Education

MEMBERSHIP: Drs. Melvin L. Cohen (Phoenix), David J. Crosby (Tucson), Boyden L. Crouch (Phoenix), William J. Dunn (Phoenix), Walter R. Eicher (Chandler), Raymond J. Jennett (Phoenix), Dermont W. Melick (Tucson), and Robert E. T. Stark (Phoenix), Chairman.

CONTINUING MEDICAL EDUCATION: Dr. Stark reported that a survey of what other state medical associations are doing in the field of continuing education has been undertaken and completed. The results were presented to the Section at its first meeting and a minute of the proceedings is of record. Uniformly, state medical associations feel that they have responsibility for and the privilege of monitoring the education of their members; that all medical societies recognize the need for continuous education of physicians; that much of the present educational effort is inadequate and unproductive; that much remains to be done; that existing programs are as different in extent and ability to present them and cooperation with members as there are medical societies. Much depends upon whether the medical association has within its confines a medical school or not, and whether their regional medical programs are becoming productive and active. Periodic relicensure and the relationship of this concept to continuing medical education is a factor as is the challenge of what is to be done regarding those physicians who do not keep up. ArMA's Resolution No. 10-69 provides for a formal report regarding the mechanics of periodic relicensure to be made at the 1970 Annual Meeting. A further survey to ascertain what medical education programs in the field of continuing and postgraduate education within medical societies in the State of Arizona is currently being conducted. Considerable discussion ensued.

It was regularly moved and carried that if periodic relicensure becomes law, the Section on Medical Education should provide the mechanism for certifying the education activities in which physicans will be required to participate.

It was regularly moved and carried that the Section on Medical Education should become the central clearing house and the certifying organization for all continuing and postgraduate activities in the state.

JCAH HOSPITAL ACCREDITATION STANDARDS: AMA files provisional draft (July, 1969) of revised standards for hospital accreditation of the Joint Commission on Accreditation of Hospitals. Substantive comment and recommendations are invited by state medical associations. It is the hope new standards will be promulgated in September and will be applicable to accreditation surveys on January 1, 1970. RECEIVED FOR INFORMATION.

TV MEDICAL PROGRAM: Discussion ensued regarding discontinuance of the TV Medical Program at either or both ASU and U of A. Dr. Flynn commented that a recent survey revealed that less than 5% of the membership is taking advantage of this educational media. Under present arrangements, it was determined by the Board to discontinue the program at U of A. It is hopeful the program at ASU may be continued under present arrangements.

Medicine and Religion

MEMBERSHIP: Dr. Wagner welcomed Dr. Robert C. Evans (Scottsdale), recently appointed a member of this Committee and designated Chairman of the Section on Medicine and Religion, who has accepted the assignment. He has been very active from the beginning of the local Ministers-Doctors Society in 1959, and it appeared logical that he should be the one to head this Section.

For the information of the committee members, Dr. Evans presented a schedule of meetings proposed by the local society of Medicine and Religion.

REGIONAL WORKSHOP: Dr. Wagner reported that Karl E. Voldeng, M.D., (Phoenix) attended the Annual Regional Workshop of State Chairmen of Committees of Medicine and Religion, held in Salt Lake City, March 29, 1969, representing Arizona in that committee meeting. Many things were discussed and suggestions made on how to conduct a program in small and large communities, how the state should enter into participation in helping the smaller communities organize getting the two disciplines, the Clergy and the medical people, together. Many will be helpful to the Section in its function next year. In addition to that, Dr. Karl Voldeng presented a meeting which was held at Tempe, at the nurses auditorium, which proved to be very successful and which was a combination of the efforts of the American Cancer Society locally and this Section on Medicine and Religion. In attendance were physicians, clergy and nurses. It was well attended and, of course, as usual primarily by the nurses, but there were a good many Pastors and Priests in attendance and also quite a few doctors. It was very well received and very well done. So the Regional Meeting in Salt Lake City definitely pricked up their ears when Karl presented this part of our program and enthusiastically agreed to suggest this to their own state committees in the western section. RECEIVED FOR INFORMATION.

Mental Health

MEMBERSHIP: Drs. Hal J. Breen (Phoenix), Richard H. Bruner (Phoenix), David S. Burgoyne (Phoenix), Gabriel L. Cata (Tucson), Robert I. Cutts (Tucson), Chairman, Hubert R. Estes (Tucson), T. Richard Gregory (Phoenix), John H. Jarvis (Mesa), Duane K. Tevis (Phoenix), Karl E. Voldeng (Phoenix), and Albert G. Wagner (Phoenix).

MENTAL HEALTH CONFERENCE: Last March 14 and 15, Dr. Cutts reported he had attended the 15th Annual Conference of State Mental Health Representatives in Chicago. The theme of the conference was mental health in children. About one-third of the participants were pediatricians. One of the keynote speakers, in fact, was Dr. Julius Richmond who is now with ODO. The focus was on pre-school child and there was some hope then of setting up a number of centers throughout the country where information could be pooled. There are a number of agencies serving the poor people, but the pre-school child seems to get neglected pretty much, especially from one to three, and it is felt that this is a source of much true and pseudo mental retardation, and it is hoped to do some better case finding, but as you know, the federal budget is not out yet and the health part of HEW is going to run third this year, it seems, behind education and welfare; so what kind of funds are going to be available we don't know. We are still awaiting a more complete report from that conference. We have not received it as yet. RECEIVED FOR INFORMATION.

MENTAL HEALTH – ALCOHOLISM – DRUG ABUSE: The next item is the visitation from the AMA Department of Mental Health. We have received a few communications from Dr. Walter Wolman, who is a Ph.D., Director of the Department of Mental Health for AMA, requesting visitation. I spoke with Dr. Wolman in Chicago last March and he said there was no hurry – this was a two year program – but we are hoping to be able to set something up this Fall in November. One of the difficulties we have is that many of the people on the Mental Health Section are also on committees in Phoenix and Tucson and the state Psychiatric Society as well as community councils or their equivalent in Phoenix and Tucson. So, there has been a lot of overlap as far as people goes, but we are trying to set a meeting up for November and invite Dr. Wolman then, and perhaps another in January or February since the mental health meeting will probably be in Chicago again in March.

The AMA Department of Mental Health is now producing a news letter, the first issue having been released in July. The AMA Council on Mental Health and Committee on Alcoholism and Drug Dependence each have a liaison representative from the Student American Medical Association. It was determined that if it be the wish of the Chairman of the Section on Mental Health such membership could be included; also, representation from nurses, psychologists, trained social workers and mental health technicians.

Perinatal and Maternal Mortality

In the absence of the Chairman, Dr. Rhu, no report submitted.

Poison Control

SYRUP OF IPECAC: Dr. Antos sought an opinion on the advisability of starting a campaign to get one ounce of syrup of ipecac into medicine cabinets, especially of families that have pre-school children. This could be a project of the Arizona Medical Association and the Auxiliary. I have spoken to a few pharmacists, and even the Arizona Pharmaceutical Association might help. The cost: twenty-five cents in individual one ounce vials; about twelve to fourteen cents when a gross or more vials involved. Effort to accomplish this objective over the past two years has been unsuccessful. Dr. Antos agreed to confer further with druggists and report back to this Committee at its next meeting, November first, outlining a program with specific recommendations.

CLINICAL TOXICOLOGY: It was reported the American Academy of Clinical Toxicology will hold a meeting in Chicago, October 22-25, 1969. Arizona has not been officially represented in past meetings. Because of budget limitations, no recommendation was forthcoming. RECEIVED FOR INFORMATION.

Public Health

MEMBERSHIP: Drs. Frederick J. Brady (Tucson), W. Scott Chisholm (Phoenix), Stanford F. Farnsworth (Phoenix), Robert S. Ganelin (Phoenix), Chairman, Bernard Levine (Phoenix) and Albert L. Rhoades (Phoenix).

RURAL HEALTH CONFERENCE: In regard to the 22nd National Conference on Rural Health (AMA – Philadelphia – March 21-22, 1969), a representative from the State Health Department did attend that meeting and did give a detailed report of it. I will forward a copy to the Central Office. There appeared nothing immediately applicable to Arizona, at least as our rural health program is at the present time. It is fairly inactive and I have been encouraging Dr. Levine, who is Chairman of that committee, to get more active in the area of rural health. RECEIVED FOR INFORMATION.

RURAL MEDICAL PRACTICE STUDY: Regarding the Rural Medical Practice Study, it is anticipated a report will issue from Mr. Kirk H. Gray shortly. It will include information on a great variety of rural health practices, use of referral centers, use of consultation within physicians, number of hours spent in the office, etc. RECEIVED FOR INFORMATION.

COMMUNITY HEALTH WEEK: Received the yearly communication from AMA regarding the 7th Annual Community Health Week (October 19-25, 1969). The topics: "Emergency Medical Identification," and "Recruitment of Health Manpower." This activity is customarily considered by the local county medical societies and they have been so notified. RECEIVED FOR INFORMATION.

PHYSICIANS AND SCHOOLS CONFERENCE: The 12th National Conference on Physicians and Schools will be held in Chicago, October 8-11, 1969. This is a very valuable meeting which we have attended in the past, and we have recommended that Dr. Jacob M. Sobol, (Phoenix), who is a member of the School Health Committee, be funded to attend that meeting.

It was regularly moved and carried that this Professional Committee provide funds for and authorize attendance by Dr. Jacob M. Sobol (Phoenix) a member of this Section, to the 12th National Conference on Physicians and Schools, Chicago, October 8-11, 1969.

ENVIRONMENTAL HEALTH: There are two items on environmental health, one — a letter from AMA which requests an opinion from our Committee about the desirability of scheduling a meeting with state association representatives from the entire country, the idea being to actually define the role of the state societies in environmental health programs. I have expressed in the past that I have been very unhappy with the fact that our Environmental Health Committee has not been at all active. The only thing that they participated in the last several years has been the air pollution matter since there has been very little in the way of real agitation or direction from other sources. Since then, it has been hard to get them active on it. I think that a meeting of this type in which general ideas are aired and possibly some direction to state medical associations is given, we try one. I would recommend that a representative be sent to the meeting. I am not sure who we should send. Dr. Ganelin was encouraged to give this meeting further consideration and submit his recommendation at a later date.

A meeting is scheduled to be held by the AMA Council on Environmental and Public Health in Scottsdale, January 9, 1970. Dr. Ganelin intends to attend and since this is a local meeting there will be no cost to the Committee.

VISION & HEARING SCREENING: Lastly, this is just a request for approval from the Institute for Human Development (which I am not specifically acquainted with) of Northern Arizona University, under the sponsorship of the Easter Seal Society of Coconino County, and with local support they intend to schedule an annual vision and hearing screening of all four year old children in the county. Official approval of Coconino County Medical Society has been given. They are asking for this state association's approval of this program. It is stated they plan to comply with guidelines as stipulated by the Minnesota State Medical Association which we discussed last year. It appears to be entirely in order and appropriate to me.

It was regularly moved and carried that the Association lend its support to this.

Safety

SCOPE OF OPERATION: Dr. Wood reported that while the Section has not met, he has been quite active attending meetings of the Governor's Committees on Emergency Medical Services and Driver's Licensure. Because of the apparent overlapping of so much of the activity between the Section on Emergency Care and the Section on Safety, it was determined the Chairmen of these two Sections get together and talk this out and come up with a specific recommendation for presentation to the Professional Committee at its next meeting.

Woman's Auxiliary

ADVISOR: Dr. Wagner called attention to the fact that we have one section that does not have a Chairman i.e. Advisor to the Woman's Auxiliary. One idea has been the selection of the husband of the then-current President of the Auxiliary. Certainly we should be alert to their needs and programs. Possibly, we could invite a member of that body to attend these meetings as ex-officio. NO ACTION.

OTHER BUSINESS

Legislation

Dr. Henry D. Smith, Acting Commissioner, Arizona State Department of Health, discussed matters dealing with legislation proposed for introduction or possible introduction in the Second Regular Session of the 29th Arizona State Legislature including: (1) an amendment to the tuberculosis control act to provide a mandate to take care of people who are considered a great degree of risk; (2) a bill dealing with sanitation, living conditions and water at migrant labor camps; (3) an amendment to the pure foods law of Arizona about forty years old dealing with adulteration of pesticides and other types of adulteration; (4) a bill to facilitate the treatment of minors with venereal diseases; (5) a bill which would provide a separate mental health program; (6) a bill dealing with immunization of children entering school; and (7) a bill dealing with industrial health — presently there is none.

Dr. Payne advised that at a recent Arizona Public Health meeting, he discussed with Representative Frank Kelley legislation recently enacted in California relating to "Quackery." He indicated he would be willing to introduce a similar bill here in Arizona.

It was regularly moved and carried that the Professional Committee request the Legislative Committee to obtain copies of the California law and discuss feasibility of writing similar legislation in Arzona.

Meeting Conduct

The Chairman, Dr. Wagner, was complimented on the manner in which he conducted the business of this meeting.

The next meeting is scheduled to be held November 1, 1969, to convene at 1:00 p.m. instead of 12:30 p.m., and it is the hope all members will be present on time to realize early adjournment.

MEETING ADJOURNED AT 3:25 P.M.

Edward Sattenspiel, M.D.
Secretary
by
Robert Carpenter
Executive Director

MEDICAL ECONOMICS COMMITTEE

Conference of the Medical Economics Committee of The Arizona Medical Association, Inc., with the Industrial Commission of Arizona at the latter's headquarters building, 2933 North Central Avenue, Phoenix, Arizona, Friday, October 3, 1969, called for 3:30 p.m.

ROLL CALL

For the ArMA Committee —

PRESENT: Drs. Armstrong, Richard S.; Brown, Harvey G., Chairman; Dregseth, Kenneth A.; Edwards, Walter V.; McGregor, Jr., John G., Ricker, John H.

Guests: Dr. Bishop, William A.; Leonard, Robert B.

Counsel: Mr. Jacobson, Edward.

Staff: Messrs. Barnett, Gerald L., Associate Executive Director; Carpenter, Robert, Executive Director; Robinson, Bruce E., Assistant Executive Director.

EXCUSED: Drs. Chesser, Ian M.; Crawford, Robert F.; Flynn, Richard O., President; Hoffmann, George L.; Landeen, Fred H., President-Elect; McDonald, Richard T.; Sattenspiel, Edward, Secretary.

For the Commission —

PRESENT: Messrs. Ahearn, John; Murphy, Frank; Thoeny, Bruce, Chairman.

Counsel: Mr. Cross, Donald L.

Manager-Claims Dept.: Mr. Nelson, Aaron W.

Secretary: Mrs. Suter, Louise.

Mr. Thoeny introduced the Commissioners.

Mr. Jacobson introduced the ArMA delegation.

Employer-Physician Reports

Mr. Thoeny introduced the first subject for discussion § 23-908 ARS which became operative January 1, 1969, providing injury reports by employer and physician (ICA Form 102). There are approximately 25,000 employers and 95 carriers in Arizona. The employer is required to furnish the employee with a card indicating the name and address of the employer's insurance carrier, the policy number, and the expiration date; the attending physician to report to the insurance carrier and the employer (with a copy to ICA). This is provided for in the law. Forwarding all copies of the claim report to ICA for distribution is the desire of the physicians. ICA does not have the distribution information necessary. The many problems involved were thoroughly reviewed. While in most instances the employee does not know his employer's insurance carrier, has no card of identification, often does not know even the name of his employer having been hired by a foreman, it was also recognized that an employee frequently is employed by an employer for only a few days, adding to the problem. ICA had no ready solution. Question as to whether some legislation is being contemplated to modify this distribution requirement specified in the existing statute brought a negative response. Apparently there is no ready answer to the dilemma. It is the hope by all parties that some solution to the problem may be forthcoming.

Freedom of Choice Procedure

ICA Rule 59(a) dealing with "freedom of choice" of physician was discussed. This provides that the injured employee shall make his first visit to the physician designated by his employer. Few employees know that thereafter they may seek permission to visit the physician of his choice — be he a doctor of medicine, a doctor of osteopathy, a chiropractor, a naturopath, or a faith healer. As to the doctor of medicine, it has always insisted that the patient should have freedom of choice among its practitioners. ICA advised it was reviewing its rules with the possibility of making some changes in line with the new law and operation. In substitution, the ArMA delegation was asked whether the Association would subscribe to the licensing of doctors of medicine by ICA qualified to care for workmen's compensation cases. It is doubtful. More study will be given to possible revision of Rule 59(a). It was conceded the employer has a definite interest in the quality of treatment rendered his injured employee to assure early recovery.

ICA Fee Schedule

Chapter 6, Laws of Arizona (1968) provides that ICA shall fix a schedule of fees to be charged by physicians attending injured employees which shall be reviewed annually by the Commission. Currently, this schedule follows the 1964 (California) Relative Value Study with a unit factor of 5.5 applied. It was stated that it has been the philosophy of ICA that unless extraordinary treatment is involved, payment for services rendered is based upon the existing fee schedule — in other words, the schedule shall not be exceeded. The inadequacy of the present fee schedule was expressed by all physicians in attendance. It was pointed out: (1) that ArMA had previously requested an increase several years ago from 4.5 to 6.0 and 7.0 on certain categories; (2) that the schedule in California at that time had been 5.5 as a minimum using its RVS; (3) that California recently requested and was granted a 6.0 minimum factor, effective October 1, 1969; (4) that the RVS was being substantially revised by California to be made available in April of next year, at which time a further unit factor revision would be requested; (5) that the 1970 RVS would take into account treatment by the various specialties, i.e., treatment by a general practitioner vs. a qualified specialist; and (6) that such specialist differential should be taken into account by the ICA.

Mr. Thoeny indicated this was the appropriate time to consider fee schedule adjustments in that premium rates are usually established by Carriers the first of the year. He stated it certainly would be difficult for the Commission to establish a unit factor on RVS in excess of that being recognized in California. To the question raised, it was indicated that less than 10% of the physicians billed their UCR when submitting claims so that it would be impossible for ICA to establish a profile on regional UCR. Such profile has not been forthcoming from ArMA and it is recognized it would not be easy to come by.

Considerable discusson ensued. In answer to a question posed by Mr. Thoeny as to the reaction of those physicians present to an increase of the unit factor to 6.0, Drs. Dregseth and Ricker responded in agreement; Dr. McGregor agreed with a differential for specialists; Dr.

Leonard would agree to a 6.5 factor based upon the American College of Surgeons views; Dr. Armstrong felt that the pathologists would be agreeable; and Dr. Bishop expressed the view that a factor of 7.0 would be acceptable, agreeing to accept 6.0 now with the understanding that further consideration would be given to the new California RVS when available. He presented a preliminary copy, but it was quite obvious that study of its new concept would be required before any conclusions could be reached.

The conference was concluded with the agreement by Mr. Thoeny that ArMA would be advised within approximately ten days of the decision of ICA as regards the fee schedule. It is the hope of the physicians that the Industrial Fee Schedule would be brought up-to-date, pointing out that in the past it has always been from two to three years behind, never current on the basis of UCR, that they have been, in fact, subsidizing the program which was never intended, and that the time is here when the doctor should be considered and granted the equivalent (under the fee schedule arrangement) of his usual, customary and reasonable fees; further, that in accordance with the law, the required fee schedule should be reviewed annually and adjusted to maintain this level.

Robert Carpenter
Executive Director

AD HOC COMMITTEE ON PROFESSIONAL LIABILITY LEGISLATION

The meeting of the Ad Hoc Committee on Professional Liability Legislation of The Arizona Medical Association, Inc., held Thursday, October 23, 1969, in the Central Office of the Association, 4601 N. Scottsdale Road, Scottsdale, Arizona, convened at 2:05 p.m., Paul B. Jarrett, M.D., Chairman, presiding.

Doctor Jarrett explained in some detail the background and purpose of this new ad hoc committee; that is, to explore areas in which improvements in the matter of professional liabilty can be made.

Mr. Howard Hassard, legal counsel for the California Medical Association, reviewed in detail the history behind the legislation that the CMA has introduced regarding professional liability. He indicated that they had eight basic areas of interest and eight pieces of legislation. When they first began their program in 1967 they found little or no interest on the part of the legislators in assisting them in introducing their bills. A most interesting phenomenon occurred during 1968 when they, in fact, had more legislators wanting to introduce their bills than they could handle. As of this date, six of their pieces of legislation have been passed and signed by the Governor. Following is a summary of each one:

Assembly Bill 574 1968 Session Chapter 1104
This law deals with the statute of limitation or the time limit beyond which a plaintiff may no longer file a malpractice suit. On the motion of either the plaintiff or defendant, the question of the statute of limitation would be tried prior to the negligence suit. If the statute had not been exceeded, then the remaining issues would then be tried.

Under this legislation lengthy, costly trials could be avoided thus saving the plaintiff and defendant unnecessary expenses.

Assembly Bill 1069 1968 Session Chapter 1122
AB 1069 would protect the proceedings and records of medical review committees of medical societies and hospitals from discovery.

With such protection, physicians would be more candid when testifying before their local committees regarding their own mistakes and that of their colleagues. Oftentimes, a settlement, rather than a lengthy court suit, is reached which benefits both parties. Additionally, a plaintiff's rights to patient records are still protected in that they can be obtained if the patient authorizes same and without filing suit.

Assembly Bill 1270 1968 Session Chapter 1129
This measure would allow an advance payment to a plaintiff for damages without such payment being construed as an admission of liability. The amount of payment would be deductible from any final settlement. The plaintiff would also be notified of the statute of limitations when receiving an advance payment.

The plaintiff, especially one with limited means, could receive early financial assistance. It is conceivable that the plaintiff would then withdraw his suit which would eliminate the need for a trial.

Assembly Bill 259 1969 Session Chapter 608
This measure, introduced to discourage frivolous malpractice suits against physicians et al for personal injury, would require the plaintiff to post a maximum $500 bond or equivalent surety, if the defendant can reasonably demonstrate that the action was instigated capriciously. If, in the opinion of the court, the plaintiff cannot afford such a bond, it can be waived.

This legislation would help to minimize frivolous malpractice suits which in turn would keep malpractice insurance rates in check. Similarly, the plaintiff is also protected in that the bond is not mandatory if he cannot afford it; further, the defendant would be responsible for paying the court fees if he is found guilty.

Senate Bill 519 1969 Session
Under this law, a second physician who is called upon to render emergency medical care arising out of prior medical care, to a patient of another physician, is not liable for civil damages as a result of any acts or omissions.

With the potential threat of a suit removed from a responding physician, the injured party is assured of treatment in an emergency situation.

Senate Bill 709 1969 Session Chapter 573
This measure provides that rescue teams, hopsitals and specified others are immune to liability for an act or mission while attempting to resuscitate a person who is in immediate threat of death, provided the team is properly trained and equipped.

Again, immediate attention can be given to a person who is in danger of death when the rescue team knows it will not be liable for a potential suit.

Two of their bills have yet to be enacted. One relates to the doctrine of "res ipsa loquitur" in which they are trying to codify this phase of the law in California. The other has to do with determining the amount of compensation or award independently of the jury who determines that malpractice has, in fact, occurred. Mr. Hassard indicated that they would make these two bills their primary efforts during 1970.

When asked which of the six bills that were passed were of the most importance in Mr. Hassard's opinion, he stated that Assembly Bill 1069, dealing with the confidentiality of medical review committees of medical societies and hospitals, was undoubtedly the most important and, in his opinion, the second most important would be Assembly Bill 1270 allowing for advance payment to a plaintiff for damages without such payment being construed as an admission of liability.

Following Mr. Hassard's presentation, extended discussion ensued between members of the committee and the invited defense counsels.

A wide variety of recommendations and suggestions were made to be considered by the committee.

At this point all guests departed and the committee went into formal session.

It was determined that at this time our main objective would be to try to get our Confidentiality of Committee Records Bill (H.B. 87) reintroduced and passed during the 1970 session. It was decided that committee members should give considerable thought to educational programs for physicians on the matter of malpractice activities.

Determination was made that consideration be given to the development of an Association committee to assist defense counsels in preparation of their cases.

The committee felt that further study and follow-up is desirable on the subject of establishing arbitration procedures in Arizona hospitals.

Finally, Mr. Jacobson is to prepare legislation along the lines of that prepared in California for consideration of the committee at its next meeting, which is scheduled for Sunday, November 23, 1969, at 2 p.m. in the Directors Room of the Safari Hotel.

MEETING ADJOURNED AT 6:35 p.m.

Bruce E. Robinson
Assistant Executive Director

PROFESSIONAL COMMITTEE

Meeting of the Professional Committee of The Arizona Medical Association, Inc. held Saturday, November 1, 1969, in the French Quarter of the Safari Hotel, Scottsdale, Arizona, convened at 1:05 p.m., Albert G. Wagner, M.D., Chairman, presiding.

MINUTE

Approved Minute of the Professional Committee meeting held September 27, 1969.

SECTION REPORTS

Aging and General Medicine

In the absence of the Chairman, Dr. Kohl, Jr., no report submitted.

Allied Medical Groups

MEMBERSHIP: No report.

MARICOPA MEDICAL SOCIETY OSTEOPATHS — MEMBERSHIP: As directed at the last meeting, Dr. Helme reported he had communicated with John C. Ballin, Secretary, AMA Board of Trustees Committee on Osteopathy, concerning admission of osteopaths to Maricopa County Medical Society membership. He was advised that the questions previously raised by Carl A. Holmes, M.D. (Phoenix) will not present significant difficulties and that efforts looking to amalgamation should be encouraged. In answer to a question from the floor, Dr. Helme stated it is now possible for a doctor of osteopathy to apply for membership in Maricopa County Medical Society. REPORT RECEIVED.

ArMA-ASNA Liaison

WORKSHOP-PATIENT CARE VELDA ROSE-MESA: Dr. Payne reported on the ArMA-ASNA Workshop Program held at the Velda Rose, Mesa, October 10 and 11, 1969. Attendance was good. It was considered a useful meeting. Open discussion prevailed throughout the session with valuable interchange of ideas. It is planned the Joint Liaison Committees will meet again shortly. REPORT RECEIVED.

AMA CONFERENCE ON NURSING: The Chairman further reported that representatives from the American Hospital Association will be included and invited to attend the Third National Conference on Nursing to be held in 1970. He feels a representative from this Association should be in attendance and stated a recommendation will be forthcoming at a later date. REPORT RECEIVED.

Athletic Medicine

In the absence of the Chairman, Dr. Toll, no report submitted.

Disaster Medicine

MEMBERSHIP: No report.

BURN AND TRAUMA UNIT STUDY: Dr. Baker reported that the Burn and Trauma Unit Study is proceeding. REPORT RECEIVED.

DRUG ABUSE: The Chairman inquired as to what is being done in the area of drug abuse. He was informed that currently there appears to be an "over kill" on the subject. Many meetings have been scheduled and held in Tucson (since 1967) and Phoenix among varying groups. Maricopa County Medical Society has a very active program in operation. Discussion ensued. Suggestions were offered to encourage programming during the 1970 annual meeting of ArMA; and to provide our physicians with some factual material available pamphlets, etc., possibly through ArMA, as an educational process. The Data Sheet released by Maricopa Society might be a good beginning toward adequately informing the doctor through statewide distribution.

Dr. Cutts under his Section on Mental Health which includes in scope drug and alcohol abuse agrees to further explore the problem.

It was regularly moved and carried that the subject: "drug abuse" be considered and included or mentioned in a panel presentation (during the annual scientific section meeting of ArMA) to which Doctors of Osteopathy are invited; and that the Program (Scientific Assembly) Committee be directed to further emphasize the role of the physician in the small community as well as the major community.

Emergency Care

MEMBERSHIP: No report.

EMERGENCY CARE-SAFETY ACTIVITY CONSOLIDATION: Dr. Schaller reported no agreement had been reached relating to the considerable overlapping of activities of the Section on Emergency Care and the Section on Safety. Possibly retention of the two Sections with dual chairmen will have to continue. REPORT RECEIVED.

TOTAL SYSTEMS DEMONSTRATION PROJECT: Dr. Schaller reported that as the result of the Highway Safety Act of 1966, Governor Williams appointed an Emergency Medical Services (EMS) Committee to develop a statewide comprehensive EMS program for the State of Arizona — this for the purpose of complying with STANDARD 4.4.11 of the Act. The Standard requires that ever state and its political subdivisions upgrade their emergency medical services so that they can provide better medical care to those injured in motor vehicle accidents. To develop the best possible facts upon which sound decisions can be based, the Committee has developed a tentative plan for a "Total Systems" EMS Demonstration Project, similar in concept to the AMES Project which is developing invaluable, and otherwise unobtainable data. It will be a test of the key components of an integrated emergency medical services system, and will involve the joint cooperative efforts of the counties and communities in northern Arizona, adjoining Interstate 40 (U.S. 66) and certain specialized hospital facilities in Phoenix and Tucson.

Dr. Schaller introduced Mr. Victor E. Rothe who is on the Staff at ASU, is also Executive Secretary of the Governor's Highway Safety Coordinating Committee and is also associated with the AMES Project, NADEC, as the project is referred to (Northern Arizona Development Council), is designed to coordinate ambulance services with the other aspects of health care in an endeavor to bring up-to-date all the services and seek group support of its concept. Dr. Schaller stated he would have a resolution to present at the conclusion of Mr. Rothe's comments.

Mr. Rothe reviewed in some detail the requirements of the Highway Safety Act of 1966. There were originally 16 Standards (now 17) and present concern is with Standard 11 involving Emergency Medical Services, designed to upgrade the quality of care including ambulance services, emergency room care, communications, transporattion, etc. It was pointed out that the Secretary of Transportation could penalize a state up to 10% of its highway construction monies which, in Arizona, could amount to ten million dollars, if such program is not carried out in a reasonable period of time. The Governor appointed an EMS Committee which membership composite totals some 50 persons having special qualifications in the various services. Subcommittees have been established. Development of proposed standards is in progress including transportation, communications, hospital care, etc., with local involvement in the problem. Seven counties have already in development EMS Committees and programs.

The development of the AMES Project appears to be highly successful. Since May 20, 1969 to date, 493 missions have been flown, 152 evacuation missions completed; 156 people evacuated; in addition to 341 other missions flown involving 708 hours. Recently the project received a 3 months extension on the flight phase. It is planned a helicopter will be based out of Flagstaff for experience during the snow season.

In the five northern counties, a Total Systems Demonstration Project is planned, back-stopped or supported with special care facilities which exist in Phoenix and Tucson, specifically the Burn Center, the spinal injury and the Neurological Institute in the Phoenix area. Mr. Rothe reviewed the details of the project in the several areas being programmed and funding. Endorsements of the program have been obtained in the five county regions including the hospitals, the county supervisors, and the medical groups. It is desirable to operate the program over a two year period. It is estimated to cost between one and one-half and two million dollars, hopefully all federally funded.

It was regularly moved and carried that whereas, the death rate in rural areas is four times greater than in urban areas, and whereas, the NADEC concept offers an excellent opportunity to update all forms of emergency medical services including patient delivery systems, first aid training, accident and injury identification and emergency communications, that this group support the NADEC concept and recommend to the Board of Directors that they give the support of The Arizona Medical Association to this project.

DRIVERS LICENSING LAW AMENDMENT: Dr. Schaller reported that in connection with the Driver License Law, the Medical Advisory Board proposes that the present Driver License Evaluation System be updated so that (1) the applicant fill out some sort of a medical history form when he makes application for license; (2) updating the physical evaluation of that person by the driver license personnel to whom he makes his license application; and (3) requiring a little better observation of his ability to drive the car from a physical or mental or emotional standpoint to be made by the driver license examiner. He reviewed in some detail procedure contemplated in the instance of a more complete follow-up requirement. REPORT RECEIVED.

Industrial Health

MEMBERSHIP: No report.

INDUSTRIAL HEALTH — INDUSTRIAL RELATIONS — MEDICAL ECONOMICS — ACTIVITY CONSLIDATION: Dr. Ryan reported action had been initiated to clarify the specific functions of the Section on Industrial Health, the Industrial Relations Committee and the Medical Economics Committee in the hope of resolving overlapping which might exist between the three groups. AMA has been contacted and information received to be evaluated. It is planned soon to contact Harvey G. Brown, M.D., Chairman of the Medical Economics Committee, who has been involved in negotiations with the Industrial Commission of Arizona. Possibly a report will be presented at the next meeting of this committee. REPORT RECEIVED.

Medical Education

CONTINUING EDUCATION: Dr. Stark reported that Dean DuVal (U. of A. College of Medicine) is actively seeking an individual to head up the Department of Continuing Education at the College of Medicine. This Section supports this enterprise and presented the following resolution which was adopted:

RESOLVED, that ArMA support and encourage Dean DuVal in his efforts to establish a department of continuing education at the University of Arizona College of Medicine.

The Chairman further reported there was discussion about participation of ArMA in a tripartite effort with the College of Medicine and RMP to establish programs in continuing education and presented the following resolution which was adopted:

RESOLVED, that ArMA cooperate with the University of Arizona College of Medicine and the Arizona RMP in a tripartite effort to organize, design and develop a comprehensive continuing medical education program for Arizona physicians.

The Chairman further reported on the results of survey undertaken to ascertain the extent of continuing education programs for physicians now being conducted. AMA has encouraged involvement. Possibly the response received from the Specialty Groups was best. Next were those received from hospitals having teaching programs. It is the view of the Section it should assume a supporting role with the University of Arizona College of Medicine and RMP in comprehensive continuing education. Dr. Stark reviewed in some detail the programs being presented by various groups. Discussion ensued. REPORT RECEIVED.

Dr. Wagner, associated part time with RMP reviewed staff discussion yesterday on a comprehensive program for continuing education in Arizona. It is primarily for physicians, but includes others such as nursing, patients' families, etc. It was a positive and helpful session. There is a desire to work with physicians and the medical school to help get the program going and keep it going. REPORT RECEIVED.

Medicine and Religion

MEMBERSHIP: Dr. Evans reports he has made contacts. Reverend Leon Glenn (Scottsdale) will continue as Secretary: Karl E. Voldeng, M.D. and Martin L. List, M.D. (both of Phoenix) will continue serving; and a new member Pastor John Pope (Phoenix) has indicated willingness to serve. REPORT RECEIVED.

EXHIBIT: At a meeting held recently it was decided members will be available to man a booth, if available, during the ArMA annual meeting, similar to that conducted two years ago. Hope also to set-up a committee meeting during that time and possibly obtain members from other county committees. REPORT RECEIVED.

REGIONAL WORKSHOP: The AMA Regional Workshop on Medicine and Religion will be held in Salt Lake City in March next. Dr. Evans hopes to attend. REPORT RECEIVED.

Mental Health

MEMBERSHIP: Dr. Cutts reported he had received positive response from six of the ten people contacted to serve on this Section and has a seventh physician candidate; also, a medical student and a psychologist. He anticipates calling an organizational meeting soon and hopes to be in a position to write Walter Wolman, Ph.D., Director of the Department of Mental Health of AMA to visit with his group soon thereafter. REPORT RECEIVED.

MENTAL HEALTH LEGISLATION: The Chairman attended a meeting held in Tucson, Thursday, October thirtieth, called by the Mental Health Committee of the Tucson Community Council, at which Dr. Willis H. Bower, Director of the Arizona State Hospital, brought to the group the latest releases on mental health legislation which is being revised almost daily. Representative Frank Kelley plans to present the final draft to the Legislature at its next session. It is the hope this time there will be but one acceptable bill. REPORT RECEIVED.

ARIZONA STATE HOSPITAL EMPLOYMENT OF OSTEOPATHS: Dr. Cutts advised Dr. Bower was pleased with the response from ArMA relating to the employment of Osteopaths at the Arizona State Hospital and was awaiting word from AMA and the American Boards referable to giving physicians residency credits. REPORT RECEIVED.

DEPARTMENT OF PSYCHIATRY – U. OF A.: The Chairman further stated that it appears the Department of Psychiatry, University of Arizona College of Medicine, is finally getting off the ground with activity. REPORT RECEIVED.

Perinatal and Maternal Mortality

In the absence of the Chairman, Dr. Rhu, Jr., no report submitted.

Poison Control

MEMBERSHIP: No report.

SYRUP OF IPECAC: Dr. Antos withdraw his suggested "Syrup of Ipecac" program reciting disinterest among the pharmacists and unavailability of the product. REPORT RECEIVED.

Public Health

ENVIRONMENTAL HEALTH: Dr. Ganelin reported that as agreed, he had communicated with the AMA Council on Environmental and Public Health advising Arizona would be receptive to attending a national meeting on environmental health matters. He received a response to the effect that other states expressed similar interest and that in all likelihood, a meeting would be called late in 1970. REPORT RECEIVED.

PHYSICIANS & SCHOOLS CONFERENCE: Dr. Jacob M. Sobol did attend the 12th National Conference on Physicians and Schools held in Chicago, October 8 through 11, 1969. He submitted a brief report which is on file. Possibly the most significant comment was that most of the health educators were of the opinion that health education and physical education should be divorced. REPORT RECEIVED.

HEALTH RECORD FORM: AMA advised that at the last annual convention held in New York, the House of Delegates adopted a resolution on "Standardized College Record Forms" submitting suggested sample copies. Dr. Ganelin reported he had reviewed them and expressed his preference to the form previously developd and forwarded to Arizona Colleges and Universities. He agreed to forward a copy to AMA for its information. REPORT RECEIVED.

Safety

In the absence of the Chairman, Dr. Wood, no report submitted.

Woman's Auxiliary

Dr. Wagner stated he would endeavor to submit a suggestion as to Advisor to the Woman's Auxiliary at the next meeting.

MEETING ADJOURNED AT 3:10 P.M.

Edward Sattenspiel, M.D.
Secretary
by
Robert Carpenter
Executive Director

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PAIN CONTROL SEMINAR

James R. Atkinson, M.D., Chairman

ST. JOSEPH'S HOSPITAL AND MEDICAL CENTER

PHOENIX, ARIZONA

MARCH 21-22, 1969

INTRODUCTION

SISTER MARY dePAUL OBERTI
ADMINISTRATOR, ST. JOSEPH'S HOSPITAL
AND
MEDICAL CENTER

Chronic pain may be ranked as one of this Country's most common disabling diseases. Millions of man hours a year are lost through chronic pain. While scientists seek the causes and the cures of major diseases, no one knows, or even suspects, the infinite number of men, women, and children suffering from diseases and other handicaps of which persistent and inescapable pain is a part.

In certain initial stages, like stimulating the hand to withdraw from a sharp object, pain serves a useful purpose. But in its intractable debasing stages, serving no purpose, it becomes a destructive disease.

Pain is so subjective that it defies universal definition, but it is interpreted from different professional and cultural points of view. The biologist considers pain a sensory signal that warns the individual when harmful stimulus threatens injury. The philosopher has called pain "a passion of the soul," an emotional process and a moralizing influence, an attitude that closely resembles the theological concept of pain as a strong moral force.

A religious attitude toward pain as an opportunity to share something of Christ's suffering in no way should obstruct research in ways and means of controlling and eliminating pain which serves no purpose. Science must apply modern techniques and tools with diligence equal to that applied to research on diseases themselves.

We are not all equal before pain.

Most of us think of pain as something that hurts, and the quicker it can be stopped, the better.

A physician is primarily obliged to alleviate pain and suffering. Physicians generally do not like patients who do not obtain relief from powerful analgesics. The patient who continues to complain of pain after a variety of narcotics is, in essence, proclaiming that the doctor is not a very good doctor. Nor are such patients very popular with the nursing staff.

To the *sociologist,* pain and the threat of it are powerful tools of learning and of social preservation. To the *physiologist,* pain is a sensation like sight or hearing. The *psychologist* is concerned with pain in another form of perception, individual and modifiable. Of interest to the *psychiatrist* are the possible psychogenic aspects of pain. To the *research scientist,* it is a total response to a stimulus modified by all manner of internal and external conditions. To the physician, pain is a message to be decoded, interpreted, and acted upon.

The Barrow Neurological Institute of St. Joseph's Hospital in June, 1967, suggested the establishment of a Pain Clinic at St. Joseph's Hospital. Under the leadership of Dr. James Atkinson, a feasibility study was conducted, and by September, 1967, a multidisciplinary Pain Clinic had been organized for St. Joseph's Hospital. This Clinic has been set up to help in the management of pain problems, which for one reason or another are difficult to control in more routine fashion. Such problems include intractable pain problems secondary to malignancy or nerve injuries in which the primary pathology cannot be brought under control. Intractable pain problems in which the chronicity of the problem or possible psychological interaction with the pain process has made management difficult are also suitable for help in the Pain Clinic.

The Clinic consists of the following group with each individual offering support in his particular area. James R. Atkinson, M.D., neurosurgery, Herbert L. Collier, Ph.D., psychology, William B. Helme, M.D., neurosurgery, Raymond A. Huger, M.D., psychiatry, initially Stanley Karansky, M.D., and later William A. Mathews, M.D. anesthesiology, Alvin D. Sidell, M.D., neurology.

PREFACE

JAMES R. ATKINSON, M.D.

This Pain Control Seminar was an outgrowth of the activities of the Pain Clinic of St. Joseph's Hospital. In the course of working with patients seen by referral from physicians in the community, it became apparent there was a broader and more general interest in the problems inherent in the management of intractable pain. We felt honored by the response of our guest facutly. Dr. William H. Sweet, who is a pioneer in the field of pain control, spoke on the exciting initial results of a new approach utilizing nondestructive techniques in which pain is brought under control by providing a new sensory input rather than by destroying a sensory pathway. Dr. Eldon L. Foltz presented in detail the anatomic and clinical facets of the cingulumotomy procedure which he developed over a decade of laboratory and clinical work. Dr. Raymond W. Houde spoke on the clinical pharmacology of analgesics with excellent comparative aspects of various analgesic agents and their dose response relationship. Unfortunately, Doctor Houde's responsibilities precluded his preparing a manuscript in time for publication deadline. The participants from St. Joseph's Hospital were all Pain Clinic members. I would like to thank the guest faculty and participants for their industry, St. Joseph's Hospital for making the Seminar possible, and those attending the Seminar for their interest.

FEAR, GUILT, ANXIETY, AND DEPRESSION IN THE PAINFUL MAN

RAYMOND A. HUGER, M.D.

Pain is a symptom, a sensation which usually brings the patient to the doctor. The underlying cause of this pain may be: 1) Organic, 2) Psychological, 3) Psychophysiologic, 4) Psychologic and Organic.

The concept of a "pain center" in the brain is totally inadequate to account for the sequences of behavior and experiences. The concept is pure fiction unless the whole brain is considered to be the "pain center." The thalamus, limbic system, hypothalamus, brain stem, reticular formation, parietal cortex, and frontal cortex are all implicated in pain perception. It is possible for the central nervous system subserving attention, emotions, and memories of prior experiences to exert control over the sensory input.

There is a considerable amount of literature and controversy about the significance of the emotional factors in a host of painful somatic conditions, such as, the shoulder-hand syndromy, fibrositis, the various myalgias, and last but not least, the various defined rheumatisms and rheumatoid arthritis. Engel (1959) under the heading "Pain Prone Patient," describes a category of people who repeatedly or chronically suffer from one or another painful disability, sometimes with and sometimes without any recognizable peripheral change. These patients have a number of psychodynamic features in common, mostly of a sado-masochistic nature.

> One such example is a 40-year-old white female, married, with five children, who presents herself with a history of multiple physical complaints involving much pain. She had seen many physicians, counselors, and psychiatrists with no relief. Finally, however, she was able to see herself as self-punishing and with a need to be punished. She recalled her mother being this same way and realized she was doing the same thing to herself and creating a similar problem in her children. With this intellectual and emotional insight her pain resolved.

The problem of pain can also be fruitfully approached by viewing it much as one would view the task of translating a foreign language. The task is to translate from pain to diagnosis. Since no bodily disorder is found, the problem which the language of pain presents is compounded. One needs to translate and to express certain experiences, particularly those relating to intimate personal relationships and feelings into other than ordinary verbal language. This need arises largely as a result of cultural and social influences. Freud was naturally struck by the avoidance of sexual and money matters in his social milieu. We see the patient who knows, or rather has learned, that he is not supposed to complain about certain matters such as sexual and marital difficulties. These problems and many others about which he has much fear, guilt, and anxiety are not supposed to be mentioned. Even in intimate, friendly relationships discussion of such matters is not usually condoned. If there is trouble in these sectors of one's life, something of course has to give. The psycho-social pressures then become translated, so to speak, into another idiom and find expression in deritive forms, such as literary, excessive drinking, and bodily symptoms.

> An example is that of a 24-year-old patient who was referred for evaluation concerning her need for a hysterectomy due to chronic low back and pelvic pain. During the interviews much guilt, suicidal ideation, and a need to be punished for a past act was uncovered. As this was resolved with the patient, a feeling of self-worth returned, the pain subsided, and no hysterectomy was necessary.

Thus while a person may feel unable to complain about personal unhappiness, he can complain about dizziness, weakness, palpitation, and pain or itching in various parts of the body. Similarly, a physician may feel disinclined or unprepared to function as an aid to the patient in his personal troubles, but he does feel that it is his proper function to communicate with him in the language of his bodily feeling, that is, in terms of body disease. The psychiatrist's role is like that of a translator or interpreter of a foreign language. He must translate the patient's body language, for example, "I have a pain in my chest" into the language of everyday speech, "I am unhappy with my wife, husband, job, child, religion, etc." When a patient goes to a physician he does not always expect or welcome such a translation. One case I have seen recently involved such a translation.

> This was a 42-year-old female who had numerous surgical procedures over the past ten years for pain in the right inguinal and femoral areas. Four operations were performed, a hysterectomy, an oophorectomy, an exploratory for inguinal and femoral hernias, and for a lumbar disc. Each procedure relieved the pain, but it subsequently returned. Finally with psychiatric help she was able to uncover much guilt about giving birth to a deformed child. This was compounded by her mother saying she was a bad person and was being punished. The pain resulted from the patient's identification with her mother who had phlebitis of the right leg following each pregnancy. The patient's pain gradually subsided with the resolution of this conflict.

Depression often underlies intractable pain. Atypical face pain or neuralgia, chronic pain with no detectable physical cause, usually with poor localization not delineated by sensory nerve boundaries, has often been linked to depression.

> A 38-year-old white female, with two children, had six years of right-sided face and head pain for which she had surgery on the trigeminal nerve with temporary relief. Recently she had further surgery on the fifth nerve. The pain again left temporarily, then returned.
>
> The patient was married twenty years to a husband who was alcoholic and cruel. He shot himself eight years ago and accused the patient of "doing it" to him. He threatened to kill her if she ever left him.
>
> The patient's father was killed in an auto accident twenty years ago at the time of her marriage. Since she had loaned her father her car, the family blamed her for his death. The entire family of eight turned on her. Finally, her mother came to Phoenix to visit her, but three days after leaving her daughter she died. The patient blamed herself for her mother's death. As the patient was treat- with psychotherapy, her self-worth was restored, and the pain in her face was relieved.

One must differentiate between pain masking an underlying depression, and a depression due to chronic or organic pain. On paper such a distinction is simple, but in practice it can present serious difficulties and there can be no hard and fast rules in the differential diagnosis. When no organic pain is found a differentiation must be made between patients with depression following chronic pain and those with pain and depression starting simultaneously. Emphasis, therefore, is on dynamic entities such as guilt, fear, predisposing background, history of suffering, tendency to salient pain, intolerance to success, strong but unfulfilled aggressive drives, etc. Thus pain is viewed as a mode of behavior derived from and addressed to each particular patient's pattern of interpersonal relationships.

Anger is probably the most difficult feeling to show in a case of close relationships because we are fearful of hurting someone or of being hurt in return, of alienating a person, or being rejected. If a person does express anger he may feel guilt or if he represses the feeling, he may turn it into fear or depression, and eventually into pain in some part of the body previously sensitized early in his life. Many people use anger as a defense against love. Love is a more acceptable emotion but many people do not feel worthy of it. The person who is full of guilt, fear, and anxiety cannot experience love in a healthy way, but unconsciously tries to experience it in a neurotic way, many times through physical illness.

Head, chest, back, and limbs are the most common sites of pain, in that order. Associated with this pain, one or more of the following five physical signs are found: 1.) Motor deficit, 2.) Tenderness, 3.) Sensory deficit, 4.) Change in contact reflexes, 5.) Vegetative changes over the body surface. In terms of psychiatric diagnosis the following may be found: 1.) Neurosis and situational reaction, 2.) Conversion reaction, 3.) Psychotic reaction, 4.) Agitated depression, 5.) Other depressive states, 6.) Manic states, 7.) Schizophrenia, 8.) Paranoid state. One word of caution is necessary. Some people want to live with their pain, and we should make sure we know who they are before we try to take it away.

OBSERVATIONS ON A PAIN CLINIC

WILLIAM B. HELME, M.D.

Most of Dr. Helme's talk was concerned with the presentation of a female patient who demonstrated many unique considerations in the neurosurgical treatment of pain. This patient was peculiarly suited to an oral and visual demonstration and cannot be adequately presented here.

He concluded by saying, "I suppose that one of the most difficult aspects of the treatment of pain is that we have no way adequately to measure it. The chiropractors have an elaborate machine with red and green lights called a neurocalometer but we have not yet reached that level of attainment. We are completely dependent on the patient and his powers of description.

"I hope we all agree that there is an emotional aspect to pain, that the patient's reaction to unpleasant sensory stimuli has some relation to the integrity of his personality and that it is impossible to isolate pain or the patient's report of it from his psychic state. Let me emphasize at this point that I am a neurosurgeon and have not deserted to the psychiatrists. However, the case which I have presented illustrates in a unique way the importance of recognizing the existence of psychological factors before one embarks on the intriguing journey of pain surgery which now beckons to us. This case may offer a gentle transition from the men of the soma who addressed us so ably this morning to the men of the spirit who follow me on this program. I believe it also serves as a significant commentary on a pain clinic.

"I have some reservations about this type of group practice mainly because it is unwieldly and expensive to tie up five or six high-powered specialists for an hour or more on each patient. However, I am confident that this multidisciplinary approach insures that adequate attention will be directed to psychological factors.

"In conclusion let me say that all of the neurosurgical procedures described in my case presentation are well established and effective when used with good judgment and that, of course, is what neurosurgery and psychiatry and medicine are all about.

"I have been asked to say a few words about pain surgery in India from which country I have recently returned. I was not specifically studying pain there but I can say that of the many hundreds of patients I saw there, none had had an operation for pain. Whether this is coincidence or the influence of the Hindu philosophy I cannot say and I will not encroach further on the province of the gentlemen who are now due to appear."

THE ROLE OF THE LIMBIC SYSTEM IN PAIN INTERPRETATION

ELDON L. FOLTZ, M.D.

The clinical complaint of intractable pain still challenges our very best therapeutic efforts. The behavioral disability associated with complaints of persisting, chronic long-term pain varies from patient to patient and appears to be based more on the basic personality type of the patient or the degree to which that patient has been "conditioned" to pain in the past. The title of this paper — "The Role of the Limbic System in Pain Interpretation" — should not be misconstrued. The limbic system itself cannot aid in differentiating the various types of pain, such as burning, lancinating, aching, etc. — but is more specifically involved in the emotional reaction of the organism as a whole to the pain as it presents clinically. More to the point, the limbic system does have a role in augmentation of emotional responses which are based on fear induced by what this pain means — that the patient's life is endangered, or that a prolonged period of serious disability is facing the patient, and so on. Such augmentation of the emotional reaction may, in some instances, be overwhelming and become the predominant clinical factor which perpetuates the disability and under those circumstances is more important to the patient for therapeutic efforts than is actual relief of pain carried over the classical fiber pathways described and studied so well over so many years. I am sure that all of us as physicians have encountered patients in whom the complaint of chronic disabling and probably intense pain has progressed to the point that the emotional reaction and the related behavior pattern has produced incapacity in a behavioral sense. These are the patients in whom the limbic system function may have behavioral significance and in which alteration of the limbic system may improve the behavioral disability even though their chief complaint may remain one of "pain".

The limbic lobe of the brain needs anatomic and physiologic definition in order to understand its clinical implications in patients suffering from chronic pain.[11] The limbic lobe is an ancient part of the brain, presumably concerned with autonomic expression and emotion.[7, 8] It has been recognised as an entity only recently and is under continuing investigation and definition.[10, 9, 11] It is a common denominator in the brains of all mammals and consists of several cortical areas overlying association and projection fiber pathways surrounding the foramen of Monro. As shown in Figure 1, the limbic lobe in the brain of rabbit, cat and monkey surrounds the foramen of Monro. Whereas the limbic lobe is bilaterally represented, it is a centrally located lobe of the brain. Olfactory function had been considered significant for this area previously; it is now generally agreed that the limbic lobe is related to emotional experience and expression.[8] Figure 2 shows a diagrammatic representation of the limbic system in man, modified somewhat after MacLean,[7] and designates the complexity of the

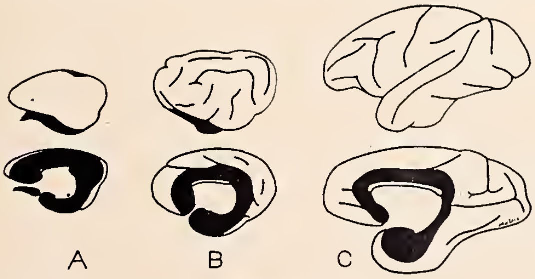

Figure 1
Limbic lobe in mammals (rabbit, cat, and monkey). (7)

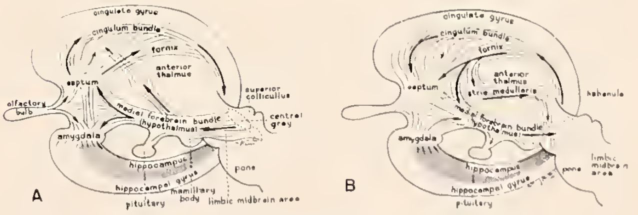

Figure 2
Diagrammatic limbic system; A — ascending pathways, B — descending pathways (7).

system. In part A, the ascending influences are depicted whereas in B the descending influences are depicted. This lobe has been studied by anatomic, evoked potential responses, and behavioral methods. Present information indicates there are extensive multi-synaptic pathways with numerous positive feedback loops in this system, arranged ideally for such function morphologically by its series of cortical areas containing cells of origin for fiber pathways interconnecting nuclear masses. It is important to point out that the cingulate gyrus and the cingulum bundle, though grossly located in what previously has been defined as the frontal lobe, are actually part of the limbic lobe and that the hippocampus and hippocampal gyrii which, though grossly located in the temporal lobe, are in actual fact part of the limbic lobe. As part A on this figure indicates, ascending influences ascend from the high brain stem via the medial forebrain bundle in the lateral part of the hypothalamus to enter the septal as well as the amygdala area. From the septum there is a possible route via the fornix toward the cingulum bundle and to temporal lobe and also via the cingulum bundle itself toward the temporal lobe. The amygdala and the hippocampus are interconnected by multiple small pathways. It should be pointed out that the influences coming up into the cingulum bundle may affect the cingulate gyrus throughout its entire course and by indirect route may also effect hippocampal action in the medial temporal lobe. In part B the descending influences may follow essentially the same pathways in the opposite direction, playing back down on limbic mid-brain areas after certain interactions have occurred, presumably at the cortex levels of the cingulate gyrus and the hippocampus as well as septal nuclei and amygdala neurons. Morphologically this entire system interconnects with autonomic effect or systems at the brain stem level in such a way as to produce and modify peripheral autonomic phenomena. In man, it is logical to associate such physiological effects with emotion. It is this system, according to some authorities, which mediates emotional responses recorded on the lie detectors, — i.e., autonomic responses to "emotionally charged" questions which ressponses are *not* controllable.

Clinical application of this knowledge of function in the limbic lobe began when the function of this lobe was shown to be essential in the syndrome of morphine withdrawal through, presumably, positive feedback or augmenting influences in the emotional sphere.[3] Interruption of the cingulum bundle in the rostral end in addicted monkeys and in human addicts extensively modifies the withdrawal syndrome. The withdrawal syndrome itself is an autonomic hyperreactivity syndrome which may in actual fact, if unmodified, produce death by autonomic hyperactivity.[3] Since emotion in man is expressed peripherally or externally by the same autonomic phenomena as seen in morphine withdrawal, it then became reasonable to assume that certain clinical syndromes involving a high degree of emotional reactivity might benefit from limbic lobe lesions. Many persons suffering from severe intractable pain show this type of emotionality.

In man, modification of limbic lobe system may be accomplished by interrupting the cingulum fasciculus in certain selected cases wherein this emotional response to their disability seems overwhelming. This same operative procedure is used in certain types of psychiatric illnesses characterized by disordered affects, including manic-depressive state.[1,6] The morphologic intent of the cingulum lesions is demonstrated in Figure 3. This figure demonstrates diagramatically the median sagittal section of human brain wherein the cingulum bundle is depicted above the corpus callosum and wherein the target area for destruction is outlined by the dotted line. Such a lesion is placed to interrupt fiber pathways of the cingulum going in an axial direction which completes the circle of fiber pathways overlayed by cortex including the cingulum, hippocampus, and the uncinate fasciculus. Figure 4 shows the uncinate fasciculus and the cingulum fasciculus in a coronal section simply for morphologic or anatomic orientation. Stereotactic approach to this area is reasonably safe and has few complications. Figure 5 illustrates the miscroscopic complexity of the primary cingulum fasciculus, showing that this fasciculus is made up of fibers coming from neurons in the cingulate gyrus as well as from the supralimbic cortex. In the middle of the cingulate gyrus these fiber pathways go anteriorly and posteriorly in the cingulum, in the anterior portion they go only anteriorly, in the posterior portion of the cingulate gyrus the fiber pathways go only posteriorly in the main fiber bundle shown at 7. There are projections coming from this main A-P axial bundle which leave the bundle, cross the corpus callosum to the opposite side, or cross part of the corpus callosum and go down the septum to the septal region, or may stay on the homolateral area to go beneath the callosum to the anterior thalamus and striatum as well as fiber pathways which course more laterally to the striatum.

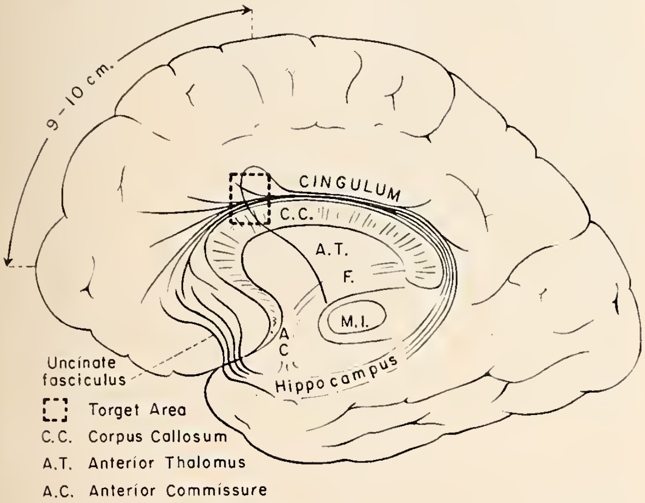

Figure 3
Coronal section diagram of rostral cingulum and its fiber pathway projections.

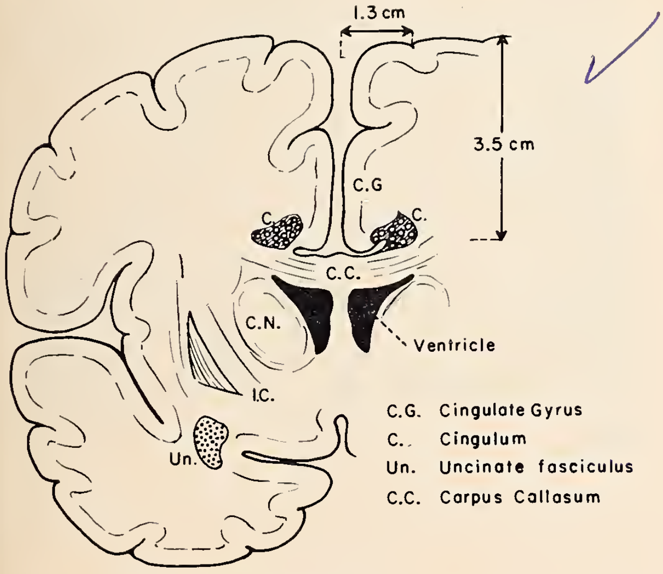

Figure 4
Median sagittal diagram of human brain to illustrate target of rostral cingulumotomy in the limbic lobe.

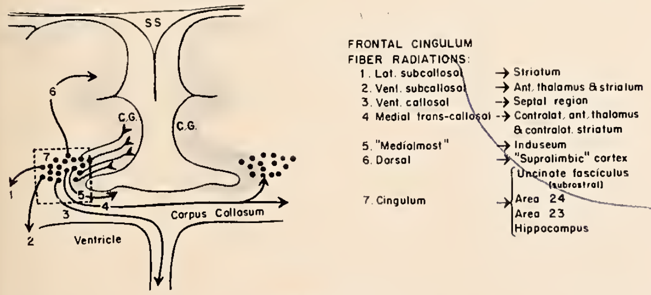
SS
6
C.G.
C.G.
7
1
5
4
3
2
Corpus Callosum
Ventricle
FRONTAL CINGULUM FIBER RADIATIONS:
1. Lat. subcallosal → Striatum
2. Vent. subcallosal → Ant. thalamus & striatum
3. Vent. callosal → Septal region
4 Medial trans-callosal → Contralat. ant. thalamus & contralat. striatum
5. "Medialmost" → Induseum
6. Dorsal → "Supralimbic" cortex
7. Cingulum → Uncinate fasciculus (subrostral)
Area 24
Area 23
Hippocampus

Figure 5
Coronal diagram, frontal, of human brain to show limbic fiber pathways (cingulum, uncinate fasciculus).

The method of cingulum destruction which we have used for several years involves the insertion of electrodes into the cingulum fasciculus as shown in Figure 6, controlled by x-ray with air placed in the ventricles so that the proper positioning of the electrodes in the cingulum bundle proper can be assured. The measurements shown on the previous diagrams hold for the x-ray alone at the time the cingulum destruction was done by radio frequency methods. Figure 7 shows the same patient with the A-P skull x-ray. The electrodes are slightly deeper than should be and were withdrawn to point Y at which point the lesions were made. The anterior-posterior position of the lesions is important. It should be emphasized in a Stage I cingulumotomy that the lesion is anterior to coronal suture line. If the clinical result is subsequently shown to be inadequate, a second stage lesion can be done as shown in Figure 8. The small air-containing space connected to the ventricles is the site of the previously made lesions in the cingulum bundle made two years prior to the second stage. The patient had recurrent symptoms of augmented emotionality to the pain problem and a second stage was therefore advised and carried out in this manner. It is important to emphasize that a cingulumotomy of this type is a relatively safe procedure to do as regards complications at the time of operation.

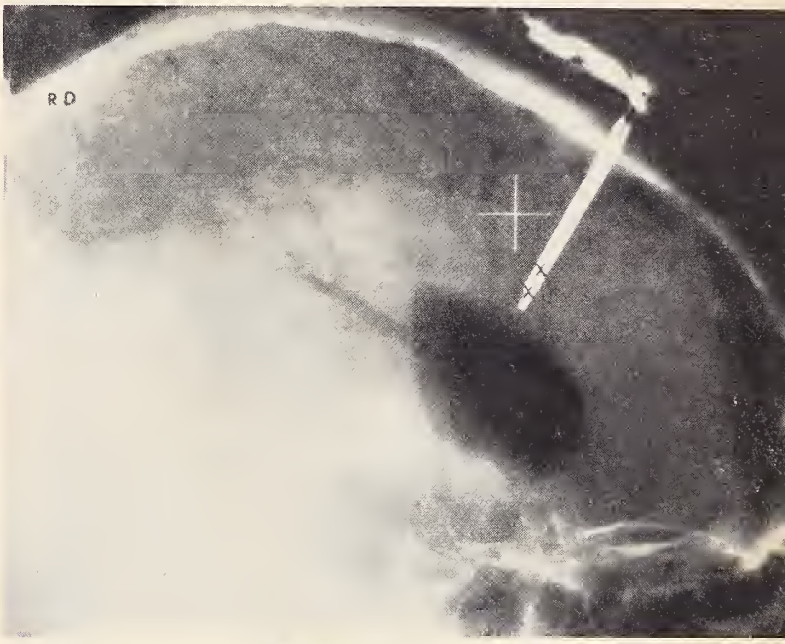

Figure 6
X-ray, lateral view, to show cingulumotomy electrodes in place; x-ray control by air in ventricles; lesion made at "X" when electrode tips slightly withdrawn.

Adequate patient selection for cingulumotomy is still the single most important criterian for a successful result.

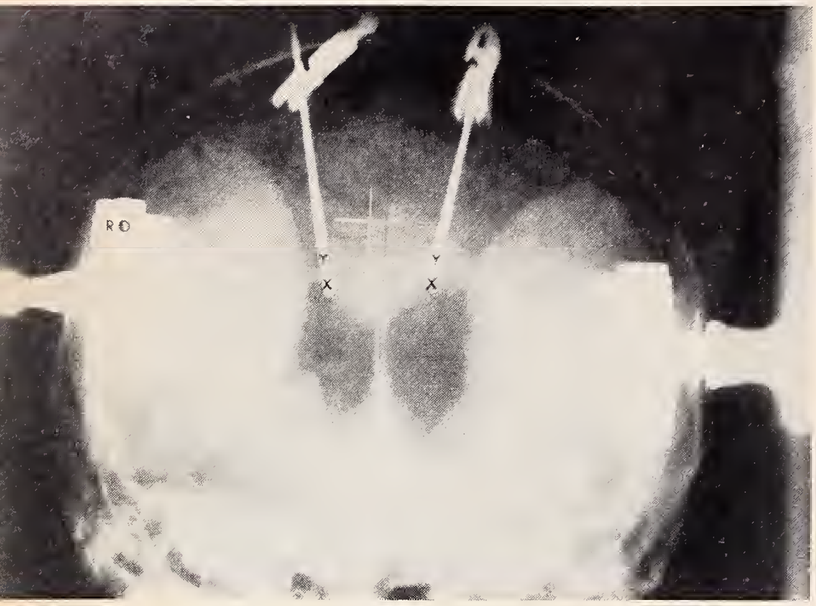

Figure 7
X-ray, A-P, of same patient as in Figure 6.

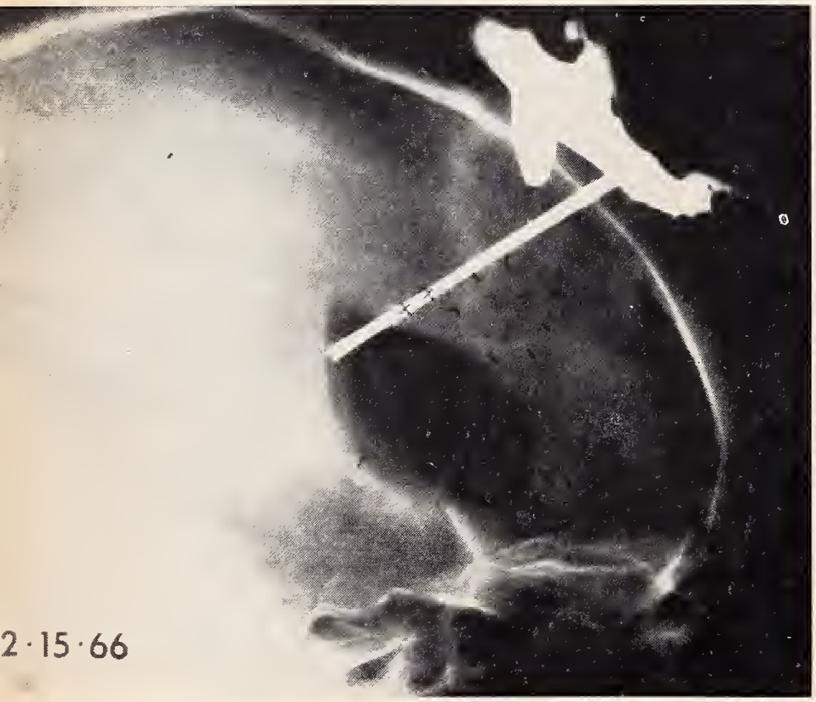

Figure 8
Stage II cingulumotomy, lateral skull x-ray; lesion made posterior to Figure 6; note porencephaly (arrows around air pocket) where previous lesions were made anterior to present electrode position.

Figure 9 shows a cross section of the cingulum fasciculus in the cingulate gyrus above the corpus callosum, a photomicrograph to demonstrate the degree of destruction in the cingulum and Figure 10 likewise shows the area of destruction done by the same manner in a group of cases reported by Ballantine[1] and confreres for psychiatric illness.

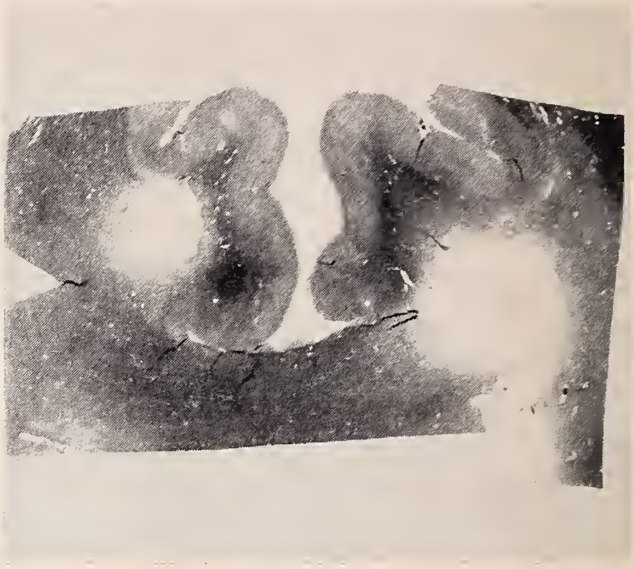

Figure 9
Photomicrograph of bilateral cingulum lesions (X).

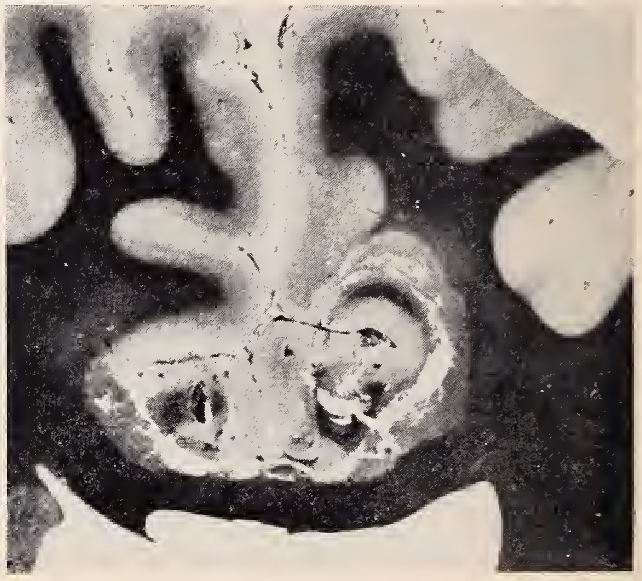

Figure 10
Photorecord of gross lesions in cingulum (Ballantine (1)).

RESULTS

In a group of 35 patients with pain augmented by emotional factors, Dr. White and I have already reported the results of rostral cingulumotomy and emphasize that the results are based more on careful preoperative evaluation and selection of patients than on any other single criterion. Selection of patients has been based mainly on our impression gained during the interview with each patient. In many instances neurosurgical interruption of primary pain pathways from the area of pain had already been done. These patients were all disabled and the actual type of pain as expressed in their chief complaint as well as the physical location of that pain were not necessarily considered critical in the decision as to whether or not the patient was a candidate for cingulumotomy. The criteria for selection were: 1) behavioral evidence of anxiety, 2) pre-occupation with their illness to the point of depression or near depression, and 3) emotional lability in the interview situation with inappropriate crying, facetiousness, etc. Where possible, psychiatric evaluation was done. In some instances we attempted to follow the criteria of patient selection as proposed by Petrie[9] wherein certain kinesthetic after-image tests of Kohler and Wallach[5] could be applied as a type of selection process. This identifies augmenter-type personalities and reducer personalities.

Figure 11 shows the manner in which we defined the clinical effects of rostral cingulumotomy in this series. *Excellent* — this indicated that no spontaneous chief complaint of pain over the follow-up period was present and the behavior was improved significantly. Many of these patients acted essentially normal for the first time in several years. A rating of *good* indicated that occasional chief complaint of pain was expressed without any need of treatment and again the behavior was improved. A rating of fair indicated that their chief complaint was present but not persistent. There may have been very little improvement, on the other hand, in their behavior. *Poor* rating involved no change in complaints, no behavioral change and those who had narcotic addiction showed withdrawal syndrome. *Worse* — there was increased complaints in suffering evidenced.

CLINICAL RATING OF CINGULUMOTOMY RESULT

Rating	Definition
Excellent	No spontaneous "chief complaint" over follow-up period; behavior improved significantly
Good	Occasional "chief complaint" expressed without need of treatment; behavior improved
Fair	"Chief complaint" not persistent; mild behavior improvement or no improvement
Poor	No change in complaints; no behavior change; narcotic withdrawal syndrome present
Worse	Increased complaints and suffering evidenced

Figure 11
Clinical rating of cingulumotomy results (2).

CLINICAL RESULTS OF ROSTRAL CINGULUMOTOMY

	Worse	Poor	Fair	Good	Excellent
A. PSYCHOGENIC PAIN	0	1	1	5+	2
B. ORGANIC DISEASE (Emotion; paroxysmal)	0	2+	2+	5+	6
C. NEOPLASTIC DISEASE (Emotional factors also)	0	0	2	4+	5+
	0	3	5	14	13

+ - 1 patient this group had unilateral lesion

Figure 12
Clinical results of cingulumotomy.

Our ratings included 35 patients. Nine patients were classified as "psychogenic pain" — and I use that term with tongue-in-cheek since "psychogenic pain" continues to mean to us a pain problem for which there is no demonstrable organic cause of the pain after thorough work-up. There were *15 patients* with organic disease of a paroxysmal nature and in which there was obvious emotional interplay. A third group was neoplastic disease in which the emotional factors were obviously present — 11 patients in this group. As you can see, we had a total of 14 *good* results, 13 *excellent* results, 5 *fair*, 3 *poor*, and none were made *worse*.

In Figure 13 the psychogenic pain group involves 9 patients with varying locations of their pain, none of which had any demonstrable local organic basis. In a second group, Figure 14, organic diseases were present and the pain was related to emotion, some of it being paroxysmal in these 15 patients. It is important to point out that three causalgia patients were included and one angina at rest, presumably on an emotional basis. These were adequately treated by the rostral cingulumotomy. Painful legs, face pain, thalamic pain and pain secondary to lumbar arachnoiditis with large emotional overlay all had good or excellent results. In the group of 11 patients with neoplastic disease (Figure 16) and pain associated with emotion, the neoplasms were in the upper extremity, the throat, face and neck as well as shoulder and arm. The emotional component to this type of pain may well have been augmented by the location of the cancer in life-threatening areas of the body, — the oral entrance and the respiratory tract.

Of these 35 patients, 22 of them were addicts. I have mentioned previously that rostral cingulumotomy does give adequate attenuation of narcotic withdrawal syndrome and all 22 of these patients who had rostral cingulumotomy, attenuation of morphine withdrawal was rather dramatic and very satisfactory indeed. There was no relationship to the clinical results, however.

Whereas we did have psychiatric diagnosis in 28 of the 35, none of these diagnoses gave a satisfactory correlation. There were numerous diagnoses of reactive depression, anxiety, depression, severe dependence, severe depression, and so on. The psychiatrists did not use terminology which was the same in the psychiatric sphere and much of their terminology was not too meaningful to us as well. It should be pointed out that the only common factor in this attempted correlation was the use of the term depression, however, which did appear in the majority of the opinions, whether written by our own neurosurgical group or by the psychiatrists involved.

A. PSYCHOGENIC PAIN GROUP:

9 PATIENTS

1 - Headache
1 - Coccydynia
3 - Face pain
2 - Vaginal-perineal pain
1 - Chest pain
1 - "Burning feet"

Figure 13
Types of "psychogenic" pain in patients treated with cingulumotomy.

B. ORGANIC DISEASE: Pain related to EMOTION
same paroxysmal:

15 PATIENTS

3 - Causalgia
1 - Angina at rest (EMOTIONAL)
1 - "Pancreatitis"
1 - Painful legs (paraparesis)
2 - Painful legs (paraplegia)
1 - Face pain ("thalamic")
2 - Hemi-body pain ("thalamic")
1 - Chest hyperalgesia
3 - Lumbar arachnoiditis

Figure 14
Patients with organic paroxysmal pain associated with obvious emotional component.

C. NEOPLASTIC DISEASE: Pain with EMOTIONAL
factors present:

11 PATIENTS

1 - Throat cancer
1 - Tongue cancer
5 - Face, neck cancer
2 - Back-hip metastases
1 - Shoulder-arm cancer
1 - Phantom limb

Figure 15
Patients with neoplasm and emotional reaction to pain.

- ROSTRAL CINGULUMOTOMY -
- ATTENUATION NARCOTIC WITHDRAWAL SYNDROME

Addicts	Satisfactory Withdrawal Attenuation	Clinical Results
22	22 (5 unilateral lesions)	Poor to Excellent*

No relationship clinical result to withdrawal effect.

Figure 16
Morphine withdrawal attenuation results from rostral cingulumotomy.

Certain changes induced in limbic lobe function by the rostral cingulumotomy can be classified as ancillary phenomena and do give some insight into the role which the limbic lobe or the limbic system may play in brain function as it relates to emotion. Figure 17 shows that we had two patients in whom relief of emotion related angina, while the patient was at physical rest, was significant following rostral cingulumotomy. Our explanation in this situation has to rest on the lessened emotional reactivity of these patients resulting in a higher threshold of emotional excitement and therefore fewer episodes of increased cardiac output demand. Under these conditions, cardiac output is more stable since the emotional status of the patient is more stable and cardiac output at physical rest is maintained at a constant level. Physical exertion *still* produced angina.

- ROSTRAL CINGULUMOTOMY EFFECTS -
ANCILLARY PHENOMENA RELATED TO
LIMBIC LOBE FUNCTION

I. CHANGE INDUCED IN LIMBIC LOBE FUNCTION:
(by cingulumotomy)
  A. Presumably increased threshold EMOTION: activation:
    1. Relief of EMOTION related angina (at physical rest) ---- 2
    2. Improved speech blockade on EMOTION activation (patients had dominant hemisphere stroke prior) ---- 2
    3. Loss paroxysms causalgic pain (EMOTION related), but persistence of joint pains ---- 2
    4. 50% decrease in insulin need in diabetic patient ---- 1
    5. Asthma attack ceased as lesion made ---- 1
    6. Marked reduction in temporal lobe seizures ---- 1
    7. Severe headache ceased; preheadache syndrome reduced ---- 1

Figure 17
Ancillary phenomena in rostral cingulumotomy patients.

In two patients a previous dominant hemisphere stroke had occurred and speech blockade was extremely marked on any type of emotion activation. The patients both could speak poorly but could be understood if no emotional activation occurred. However, when the patient became unable to make himself well understood or he became excited for some reason, almost complete speech blockade occurred and communication was impossible. Following rostral cingulumotomy, striking improvement in speech occurred because of the increased threshold to emotion activation.

As you will note at #5, one patient was treated who was having an asthmatic attack at the time the lesions were made. The asthma previously had been related to emotional upsets and under this situation the asthma attack ceased and post-operative follow-up showed that the asthmatic episodes were greatly reduced. Figure 18 shows that certain rostral cingulumotomy effects presumably came from an inbalance in the autonomic system producing an instability in what we have called "homeostatic mechanisms." The first patient listed on Figure 18 was a 35-year-old lady who had suffered a gunshot wound of the upper arm, followed by causalgic-like state, and a stellate ganglionectomy on that side had produced a Horner's syndrome for four months, associated with complete relief of her causalgia-like state of pain in the left upper extremity. Subsequently, at four months, reappearance of the causalgia-like state occurred and she was incapacitated and totally disabled at the time we saw her. She had no evidence of a Horner's syndrome at the time we did her rostral cingulumotomy for the pupils were equal and symmetrical; there was no lid droop on either side, and no evidence of loss of sweating on either side of the face and no enopthalamus. Immediately after completion of the rostral cingulumotomy, the Horner's syndrome had reappeared! She was free of her complaints of pain in the left upper extremity and remained so for six months. During this time her Horner's syndrome was persistent and then an episode occurred in the family with severe emotional overtones and for a period of several hours during one day, the Horner's syndrome disappeared and her causalgic-like pain in the left upper extremity reappeared. We have now followed this lady for 5½ years and she currently is a housewife in a pleasant Colorado town where she follows her daily routine with complete absence of the causalgic-like pain. She still has the disability from the gunshot wound of the plexus but is reasonably comfortable until she becomes emotionally upset. Emotional stresses of her life occasionally peak and at these times her own physician has noted and recorded to us that the Horner's syndrome has disappeared and she is again complaining of the causalgic-like pain of the left upper extremity and shoulder. This is transient, however, and in every instance, when the personal crises is over with, and often this is associated with some sort of sedation therapy, the patient becomes asymptomatic again and her Horner's syndrome reappears. The explanation of this sequence of events in this patient is a little difficult to define in standard neurophysiology and neuroanatomical terms. However, it is our feeling now that she had a lesion made by the stellate ganglionectomy in the lower levels of the autonomic system which produced the Horner's syndrome originally but that it disappeared ultimately secondary to homeostatic mechanisms or adjustment of higher centers to overcome those lower center deficits and maintain or place the nervous system function back in a stable balanced condition. This was possible and persisted as long as the cerebrum itself was intact, but when the rostral cingulumotomy destroyed limbic lobe compensatory mechanisms in this system, then the Horner's syndrome reappeared and this, of course, was associated with relief of pain as it was in the initial operation. This has a strong suggestion that the limbic system is directly related with lower autonomic centers and that if lower autonomic centers have already been destroyed by a lesion, a second lesion in the limbic lobe itself may be surprisingly effective and produce symptoms and signs which originally we felt were possible only by destructions of the peripheral autonomic system such as by stellate ganglionectomy, etc.

- ROSTRAL CINGULUMOTOMY EFFECTS -
(con't)

B. Presumably autonomic system imbalance from lesion; an imbalance in "homeostatic mechanisms":

1. Reappearance Horner's syndrome; present 2 years prior after Stellate ganglionectomy for 4 months only	1
2. Urinary incontinence, gradually controlled over weeks, not asocial behavior	4
3. Reduction in mass flexar responses (in paraparesis)	1
4. Total loss of "thalamic" face pain (prior stroke)	3
5. Phantom limb become "relaxed"; "no pain"	1
6. Hypotension (70/50) for 2 days	1
7. Post-operative seizures, symmetrical clonic-tonic, minor, for 2 days, no ictus; prior stroke	1

Figure 18
Ancillary phenomena in rostral cingulumotomy patients.

In conclusion, it is our feeling that the limbic system plays a role in normal physiology of homeostasis in the sphere of the autonomic nervous system but that in certain clinical conditions which we have described as "emotionality" this limbic system may be over-reactive, hypersensitive, or in an augmented state to the extent that feedback mechanisms have become so active that the emotional tenor of the patient now becomes dominant in the clinical evaluation of their complaint of pain. Under these circumstances, the operative procedure of rostral cingulumotomy, or any other operative destruction of the limbic system, may be clinically effective in reducing the emotionality to a more normal level by a volume reduction effect since these feedback mechanisms will be destroyed or at least distorted to the extent that such an augmented state cannot exist. This type of volume reduction of the sensitivity of the limbic system is compatible with reasonable personality behaviors and does not necessarily imply a dull apathetic person. Many of the patients whom I described to you were executives in banks, and so on, and were back at work within a few weeks of the operative procedure. Intellectual impairment has not been demonstrated in properly done rostral cingulumotomy cases.

Lastly, it is our feeling that the most important part of the patient workup in considering rostral cingulumotomy is patient selection. Such selection must be based on the personality substrate of the individual and must recognize that at the present time, our methods of selection are by scientific methods crude, and yet by clinical measurements are still based on a clinician's estimate of the basic personality, that is whether the patient is an augmenter, a person or a reducer person who is suffering a great deal of pain in silence and now showing overt emotional reactions or autonomic phenomena associated with such. Much remains yet to be done as further efforts continue to find better selection methods. Such methods must take into account, however, the entire or total patient and his reaction to the life-threatening process which has produced intractable pain as his primary symptom.

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STEREOTAXIC APPROACHES TO PAIN PROBLEMS

The development of functional neuroanatomy over the course of the last century led to the realization that some patients with intractable pain could be relieved by interruption of specific areas and pathways of the brain and spinal cord. Unfortunately, these areas of surgical interest for pain control lie deep within the body, and conventional surgical approach required involvement of many overlying structures. Stereotaxic neurosurgical procedures have been developed over the last 20 years to meet the need for techniques which would allow approach to and destruction of structures deep within the nervous system with minimal involvement of intervening tissues.[1]

There have been many devices developed to permit reaching parts of the nervous system not under the surgeon's direct observation. The basic approach is quite simple in all cases. A three axis cartesian coordinate system or a system of cartesian and polar coordinates is established for the patient, and the head is fixed with respect to the system. The area of interest within the nervous system is identified by proximity to radiographic landmarks, often with the help of contrast media. An electrode or probe is brought to the target from outside the body, traversing skin, bone, and any other intervening structures with minimum disruption.

The probes often contain multiple elements to allow physiologic recording, stimulation, and temperature control before or during lesion production. When the target has been identified radiographically and physiologically, a lesion is produced utilizing an external energy source directed through the probe to the tip. Early workers utilized a simple mechanical system with an extendible loop at the probe tip which would be swung through an arc to make a lesion. More recent energy sources have been cold[2] in the form of liquid nitrogen ("cryosurgery") or electrical energy[3] (converted to heat or through electrolysis) for lesion production.

Useful clinical application of these techniques has been rapid in the last decade, reflecting the work of many pioneering men in the field. We have a broad spectrum of procedures to choose from, a few of which I would like to mention briefly.

Cingulumotomy, which was developed by Dr. Foltz, and which is described in detail in his section of the Seminar, has been utilized at the Barrow Neurological Institute in its bilateral form 25 times in the last five and one-half years. There have been no operative deaths or significant surgical complications. Long-term followup indicates two-thirds of the patients have been significantly helped. Our major problem in the application of this procedure, as in Doctor Foltz's experience, is in the area of patient selection. Doctor Collier's help and interest in this area have been of great importance, and are described in some detail in his section of the Seminar.

Percutaneous cordotomy techniques were introduced at the Barrow Neurological Institute in March 1966. Early procedures relied heavily on x-ray control for electrode positioning.

As experience with the new techniques increased, physiologic localization aids such as stimulation, recording, and tissue impedence changes have been added. Better control of the radio frequency currently utilized to produce the lesions has been reflected in steadily improving results.

Eighty procedures have been undertaken in this three year period; 44 from the lateral approach described by Mullan[5] and Rosomoff[6] in which the electrode is introduced between C_1 and C_2 anterior to the dentate ligament, and 36 from the anterior transcervical approach described by Lin.[7] Eleven patients had bilateral lesions.

Satisfactory pain control has been obtained in 86%of the group. Complications occurred in 15% and ranged from the production of Horner's syndrome in some of the C_{1-2} lesion cases to more serious problems such as extremity paresis and sphincter involvement. There were two deaths related to the procedure, and 19 patients in the group have subsequently expired. Most of these deaths were due to the neoplasms which had produced the pain requiring the procedure.

One of the major problems in the stereotactic cordotomy procedures results from the anatomic proximity of the pain pathway and descending motor pathways in the spinal cord. These structures are only 5 mm apart, and overlap of the pathways, or lesion extension to the motor system is still a problem. Further research is currently underway at the Institute to provide better lesion control, and a conjoint project is underway with our neuropathologist, Dr. John Waggener, to better define lesion morphology.

Another useful procedure is percutaneous descending trigeminal tractotomy. In this procedure a lesion is made in the medulla to divide the descending trigeminal system. The proximity of vital centers limits application of the procedure to patients with naso-pharyngeal carcinoma or tic douloureux who are too ill to withstand open surgery. We have utilized it in seven cases.

Other stereotactic procedures such as thalamotomy and mesencephalotomy have been useful but our experience with them is too limited to report at this time.

In summary, stereotaxis has provided a useful adjunct to neurosurgical pain control procedures. Many patients who formerly would have been beyond any type of effective pain control can be helped. Problems in patient selection for a given procedure are difficult, and will become more so as the number of options open to the patient and his surgeon increases.

The potential hazard inherent in all of these procedures is due to their basically destructive nature. As better lesion control and target location techniques are developed, further reduction in unwanted side effects will follow. Despite these problems, I feel stereotaxis, carefully applied, in properly selected cases, is a valuable tool in mankind's continuing battle against pain.

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CONTROL OF PAIN BY FOCAL ELECTRICAL STIMULATION FOR SUPRESSION

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JAMES G. WEPSIC, M.D.

The widespread importance of peripheral and central inhibitory phenomena in the nervous system has been appreciated mainly on the basis of animal studies in the past 10 years. In 1961 for example, there was an International Symposium on Nervous Inhibition. However, little of the flowering knowledge on inhibition deals with pain since this subjective phenomenon lends itself only with great caution to experimental analysis in animals.

But in man two pertinent groups of clinical observations were made over 40 years ago which bear upon the problem of suppression of pain by activity in large myelinated fibers (Head, Rivers and Sherren, 1905;[1] Förster, 1927 p. 13-15).[2] During the early phase of recovery after division and suture of a cutaneous nerve, pain is at first the only sensory modality evokable by any stimulus noxious or non-noxious. This pain provoked even by touch has pecularly unpleasant, long lasting, irradiating features, subsumed under the term hyperpathia. In this painful phase of regeneration the nerve contains few or no larger axons with thicker myelin sheaths. Their later appearance is correlated with disappearance of the hyperpathia. Likewise after herpes zoster the hyperpathic response to touch and the spontaneous severe pain are associated with a huge increase in the ratio of thin to thick fibers in the afflicted nerves. (Noordenbos, 1959).[3]

And in the human spinal cord there may be a constant, suppressor influence on pain related to the heavily myelinated posterior columns. Förster (1927, p. 77-78)[2] has had two convincing cases with intramedullary masses in whom his incisions into a posterior column were followed by ipsilateral hyperpathia and spontaneous pain from the segmental level of his incision on down.

The work of Wall and colleagues has provided us with a possible clue as to how the input in the large, fast-conducting fibers interacts with that from the small, slowly-conducting fibers. Fig. 1 helps us review the pertinent anatomy in a section of the lumbar spinal cord. In the diagram at the bottom, the rectangular slab represents the substantia gelatinosa, and one sees that terminals of both the fine and the coarse fiber input are related to the arborizing dendrites of the secondary afferent neurones, represented as black spheres just ventral to the substantia gelatinosa. Mendall and Wall (1965),[4] recording from axons of single cells in the larger of secondary afferent neurons in the posterior horn of the spinal cord, have selectively stimu-

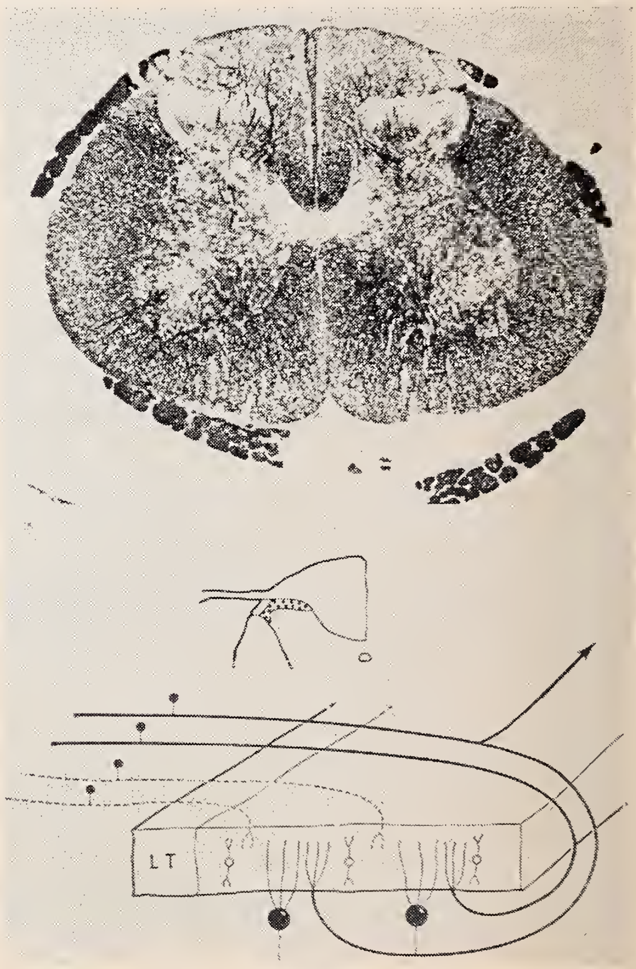


Figure 1
Anatomy of sensory fibers entering spinal cord. Top: Myelin-stained cross-section of a cat's lumbar spinal cord. Middle small diagram: Cross section of left dorsal quadrant (substantia gelatinosa stippled). Bottom: Main components of cutaneous afferent system. From Melzack and Wall: Science, 1965. Courtesy of the editor.

lated either the large, low threshold A fibers, or blocking these by anodal polarization, have stimulated only the smaller C fibers. Both types of fibers feed into and fire a single cell in the secondary afferent neurone category. (Fig. 2) Each of a succession of A fiber stimuli causes a brief burst of axonal spikes followed by a brief period of inhibition of the spontaneous firing pattern. (Fig. 3) A succession of C fiber stimuli on the other hand produces a progressive build-up in the number of spike discharges ensuing after each stimulus.

Turning from these animal studies to man, Wall and I (1967)[5] asked ourselves if artificially intense stimulation confined to the low threshold A fibers could usefully reduce clinical pain. We first tested ourselves, sticking into our own infraorbital nerves needle electrodes insulated except for the tip. Square wave pulses at 0.1 msec. and 100 cycles/sec. evoked tingling, buzzing or vibrating sensation in some portion of the sensory domain of the nerve at voltages near the threshold. These were not unpleasant feelings and were always tolerable for an indefinite period. Striking to us was the fact that we each had hypalgesia to pin prick in this area of paresthesia during the stimulation. But, both the objective sensory loss and our subjective sensations returned rapidly to normal when the stimulus stopped.

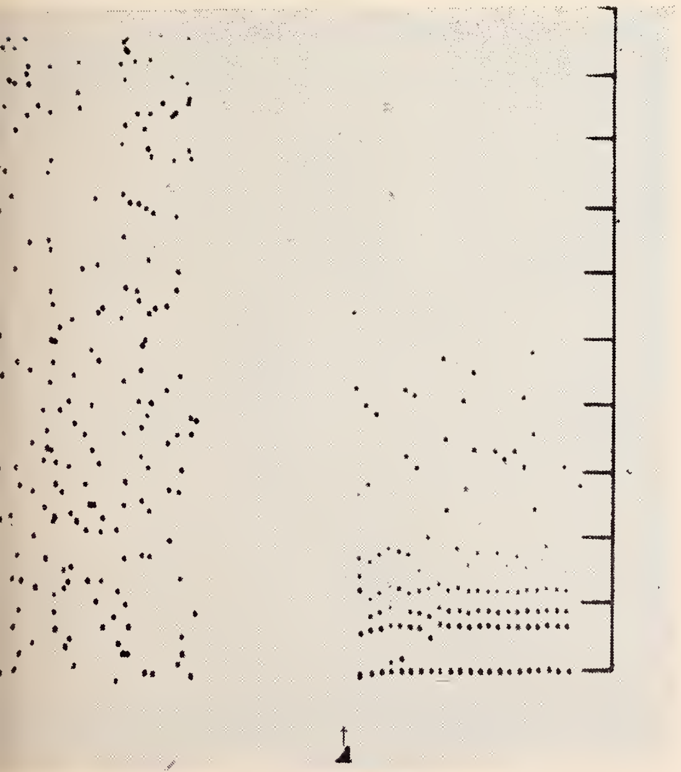


Figure 2

Spike discharge of a single axon of a large cell in dorsal horn of spinal cord. Left: Random spontaneous activity displayed as a series of vertical columns lasting one second. Right: Activity evoked by stimulation of sural A fibers. From Mendell and Wall: Nature (1965). Courtesy of Fisher, Knight & Co., St. Albans.

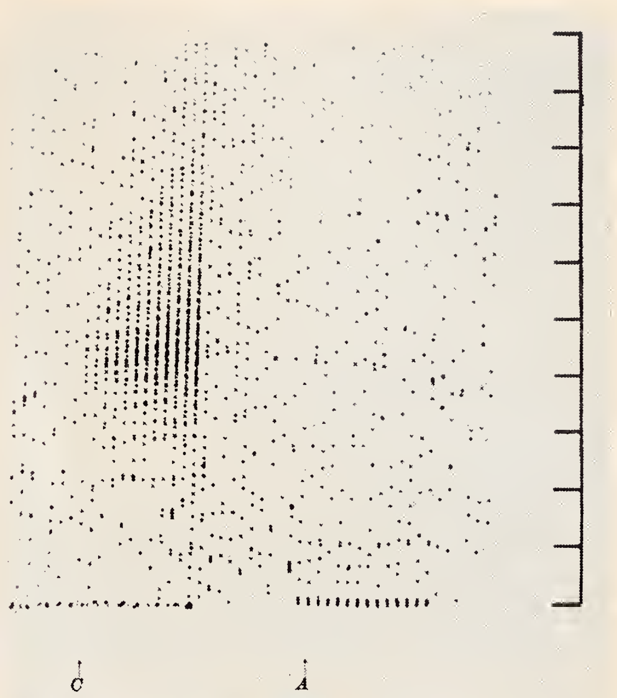


Figure 3

Spike discharge of a single axon of a large cell in dorsal horn of spinal cord. Left: Activity evoked by stimulation of sural C fibers alone. Right: Activity evoked by stimulation of sural A fibers alone. From Mendell and Wall; Nature, 1965. Courtesy of Fisher, Knight & Co., St. Albans.

With this fragmentary encouragement we proceeded in the summer of 1965 to patients with chronic pain poorly relieved by narcotics or by previous neurosurgical operations. Our 31 patients have suffered from a wide variety of disorders from typical trigeminal and atypical facial neuralgia to pain from phantom limbs, spinal arachnoiditis, and advancing malignant neoplasm. Pain from lesions within the cord, especially that following cordotomy has particularly attracted our attention because of the difficulty in relieving this by standard procedures.

Stimulation of large fibers by externally placed electrodes or vibrators has usually been followed by skin sensitivity or decreasing effectiveness leading us to implant electrodes and radiofrequency receivers. However, one patient has been able to control the pain of 2nd division atypical facial neuralgia for two years by relatively brief applications of ball-tipped electrodes at the infraorbital foramen.

In 12 patients we have implanted platinum electrodes encased in silastic and connected to a radiofrequency receiver button. (Fig. 4) The size of the unit is indicated by the penny. Fig. 5 shows the unit with the electrodes around the ulnar nerve low in the arm and the receiver high on the medial aspect of the arm. Fig. 6 shows the doughnut antenna which when in operation lies on the skin surrounding the subcutaneous receiver button. The stimulating unit permits one to vary pulse width, frequency, and power.

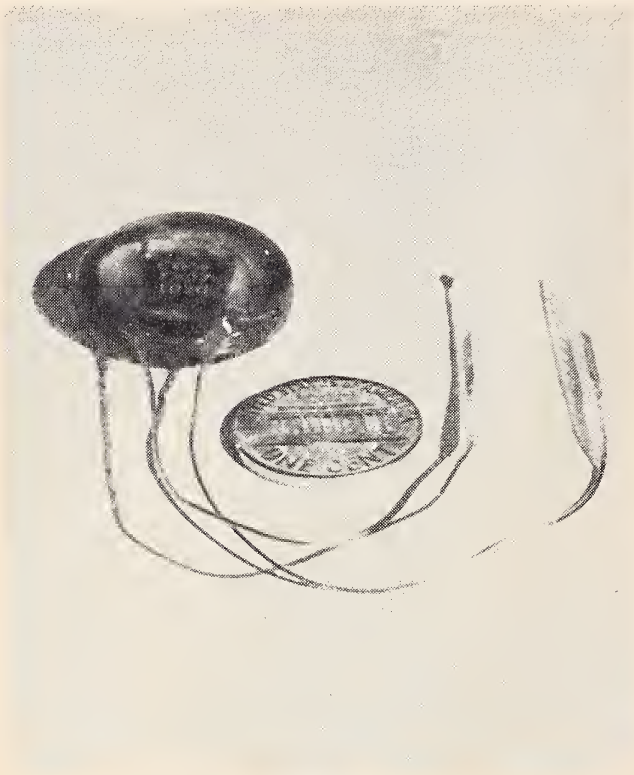


Figure 4
Receiver connected to electrodes for subcutaneous implantation in man. A United States penny (diameter 1.85 cm) is included to indicate the size of the unit.

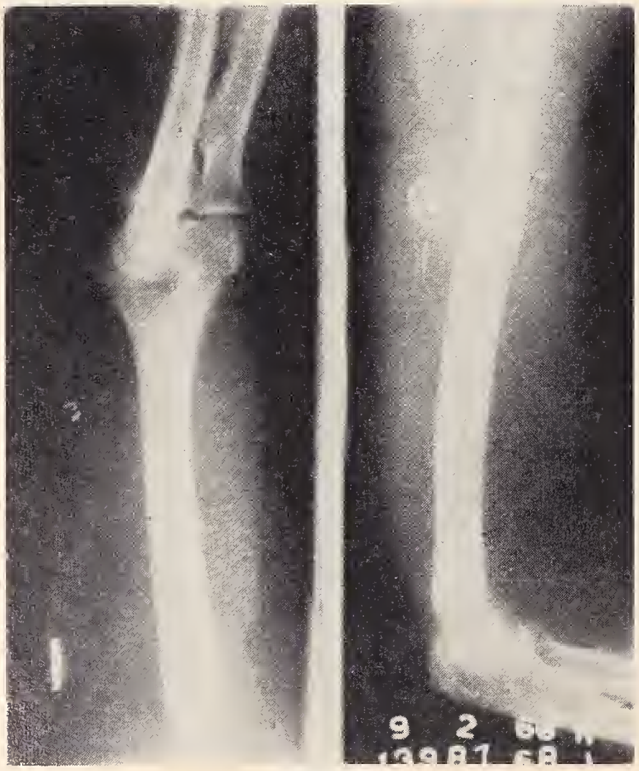


Figure 5
Subcutaneously implanted unit in middle third of arm of patient Kenneth S. (Case 1709). Receiver placed just below axilla.

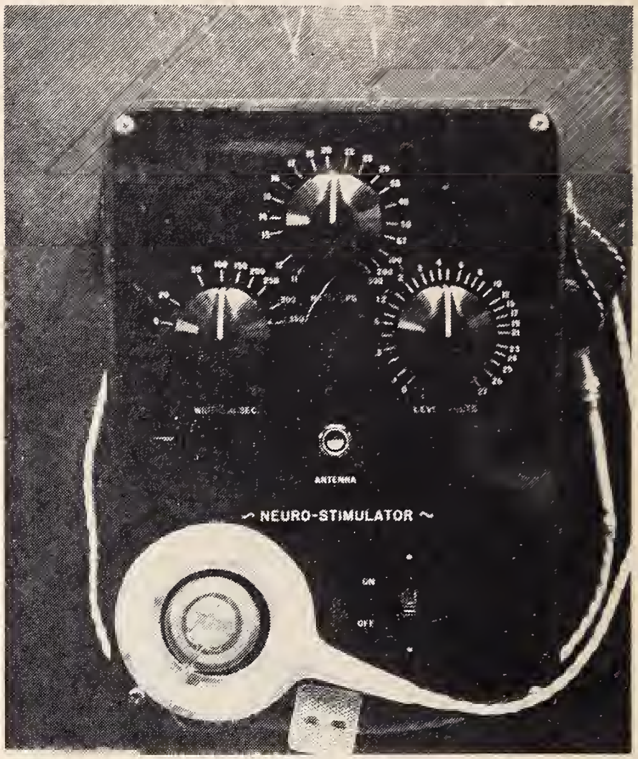
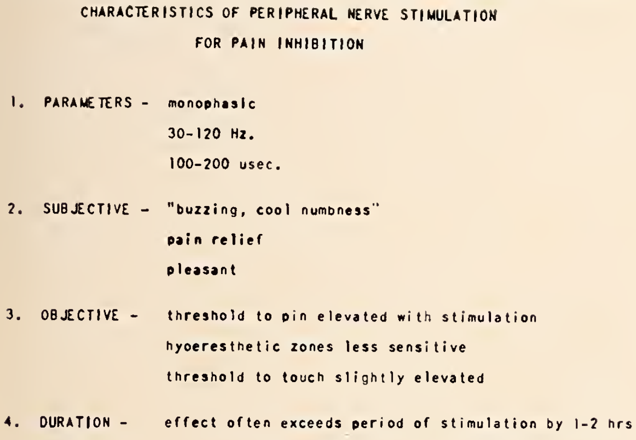


Figure 6
On the bottom: The white ring is a plastic-covered doughnut-shaped antenna which is applied to the skin overlying and surrounding the subcutaneous receiver. The white cord leads to the stimulating unit. On the top: Our master stimulating unit which permits independent variation of pulse duration, pulse frequency and voltage. In the smaller stimulator given to the patient, we set the pulse frequency at the optimal level for him, but he can vary pulse rate and voltage.

Using this flexible stimulator post-operatively we systematically define the best parameters of stimulation to inhibit pain. Once these are determined, the patient is provided with a small battery-powered generator tuned to "his parameters." He takes this unit home with him and stimulates as often as necessary to control his pain. Some patients including those with spinal cord electrodes have a stimulator which, in addition to control over power, allows them to vary the frequency of the stimulus, for we have found that especially in the posterior columns, pain inhibition may fail after prolonged stimulation at one frequency while it may be entirely satisfactory at a slightly higher or lower frequency immediately thereafter. Thresholds for effective stimulation have usually been found to be constant suggesting little reaction at electrode sites.

Peripheral nerve seems to respond best to monophasic stimulation at frequencies from 30 to 120 herz (CPS) with pulse durations of 100 to 200 microseconds, although the latter variable has not been crucial (Fig. 7). The patients with these electrodes describe the feeling with stimulation as a "buzzing" or "cool numbness" in the affected area and these feelings occur well in advance of motor activation in mixed nerves. The sensation is not uncomfortable. In both painful and non-painful areas of a given stimulated nerve's distribution, the threshold to calibrated pin is elevated with stimulation. A 2-6 gram pin application may feel sharp without stimulation, while 10-20 grams are required to produce sharpness with stimulation. Hyperpathic areas become able to tolerate more vigorous stimulation with calibrated hairs and frequently it is impossible to demonstrate any hyperpathia during stimulation even though stimulation with as little as 10 mgm. hairs produced paroxysms of pain without it. Usually the patients state that their pain is not "completely gone" but rather that with stimulation it is better, bearable or masked. Thresholds to light touch are slightly elevated although these changes have not been troublesome clinically. Position sense has not been measurably affected by peripheral nerve stimulation although if one varies the frequency of stimulation quickly, the patient may have the feeling that the innervated area is moving. An important finding in most patients, unexpected on the basis of our own infraorbital nerve stimulation, was that the pain relief pursuant to stimulation often lasted for several minutes to hours after termination of stimulation.



CHARACTERISTICS OF PERIPHERAL NERVE STIMULATION
FOR PAIN INHIBITION

1. PARAMETERS - monophasic
30-120 Hz.
100-200 usec.

2. SUBJECTIVE - "buzzing, cool numbness"
pain relief
pleasant

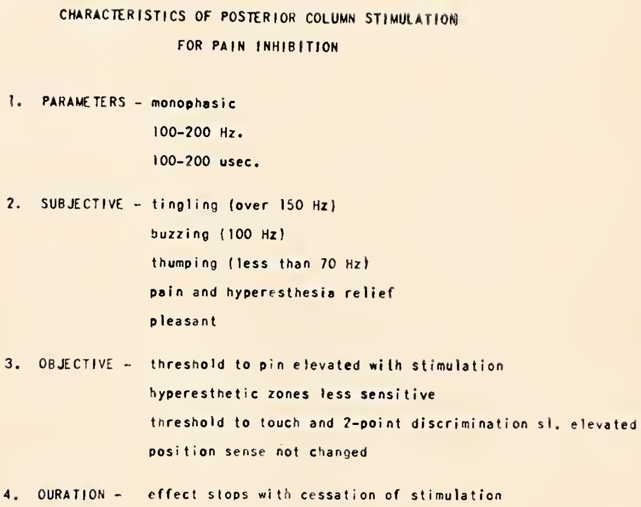
3. OBJECTIVE - threshold to pin elevated with stimulation
hyoeresthetic zones less sensitive
threshold to touch slightly elevated

4. DURATION - effect often exceeds period of stimulation by 1-2 hrs

Figure 7

Characteristics of peripheral nerve stimulation for pain inhibition.

Chronic spinal cord stimulation first carried out by Dr. Shealy and colleagues (1967) has been used by us in five patients (Fig. 8). Extended evaluation of three of them demonstrates the following points: 1) Elevation of thresholds to calibrated pin occurs in the area stimulated; 2) Both hyperpathia and pain can be relieved by stimulating; 3) Effects of stimulation cease a few seconds after its termination as opposed to sustained peripheral nerve effects; 4) Continuous stimulation can be carried out without clinical impairment of motor-sensory functions. Although two point discrimination and light touch perception with calibrated hairs are slightly decreased during stimulation with regard to control values, this loss has not been of practical significance. Electrode motion with changes of position and respiration has not been encountered with the current electrodes placed extra arachnoidally but subdurally and tethered internally to the dura bilaterally.



CHARACTERISTICS OF POSTERIOR COLUMN STIMULATION
FOR PAIN INHIBITION

1. PARAMETERS - monophasic
100-200 Hz.
100-200 usec.

2. SUBJECTIVE - tingling (over 150 Hz)
buzzing (100 Hz)
thumping (less than 70 Hz)
pain and hyperesthesia relief
pleasant

3. OBJECTIVE - threshold to pin elevated with stimulation
hyperesthetic zones less sensitive
threshold to touch and 2-point discrimination sl. elevated
position sense not changed

4. DURATION - effect stops with cessation of stimulation

Figure 8

Characteristics of posterior column stimulation for pain inhibition.

In conclusion: We are obviously somewhat encouraged by our results or we should not have persisted in this type of treatment with 31 patients. However they represent such a diverse group of syndromes of intractable pain, and our period of observation is still short enough so that we are prepared at this point only to recommend this as a potentially useful addition to our armamentarium in the management of pain.

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PSYCHOMETRIC CONSIDERATIONS IN PATIENT SELECTION FOR PAIN CONTROL PROCEDURES

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Introduction

Prior to the inception of the Pain Control Clinic, psychological testing had become a part of many patients' pre-neurosurgical diagnostic evaluation. This emphasis towards multi-dimensional evaluation is consistent with the idea of considering the "whole man" in contrast to what we frequently see as a more specified and limited study.

My own interest in participating in such a multi-disciplined evaluation pre-dates my association with Barrow Neurological Institute and the Pain Clinic to the time when I was in training and later a member of the Staff of the Medical Psychology Department at the University of Oregon Medical School. There, psychological evaluations were frequently a part of pre-major surgical studies. Typically the kinds of questions surgeons were concerned about had to do with the adequacy of the individual's psychological make-up including his various defense mechanisms, life style, self-concept, and perhaps body image to deal with the very imposing threat that major surgery sometimes presents to patients. Since surgery has become increasingly elaborated and sophisticated over the years and with the advent of implantation of mechanical devices as well as organ transplants, psychological considerations need to play a role in assuming some responsibility for making decisions as to whether or not a surgical candidate will be able to handle the changes that these procedures bring about.

I would like, therefore, to describe my role and outline what contribution the psychological evaluation can make in evaluating patients for pain control procedures. This discussion will describe our efforts toward making better predictions as to which patients will be able to cope with and benefit from a variety of surgical procedures as well as assessing what effects the procedure has had.

My participation for example in the evaluation of Cingulumotomy candidates had a two-fold purpose: 1) There was a need to discover empirically which of the many psychological tests would be sensitive enough to detect differences in individual's mental functioning following a Cingulumotomy procedure, and 2) which of the tests would be helpful in predicting what particular type of candidate would be likely to be more successful in adapting to the procedure. For that reason I felt it necessary initially to include as broad a test battery as possible in order to maximize the chances of locating significant variables. This battery included a general test of intelligence, and objective measure of personality, two projective tests of personality, a test designed to measure perceptual motor functioning, and a test designed to measure attention span. A clinical interview was also included.

It soon became apparent that many of the patients were unable to cope with a number and variety of procedures for several reasons. First of all, they were, by the very nature of their complaints, generally in a good deal of physical stress, they also fatigued rather readily, and many of them had physical limitations which prevented them from participating in the full battery. For example, some of them were physically involved to the point where they could not utilize their extremities in paper and pencil tasks.

Composition of the Test Battery

The scope of the evaluation was broad. We were measuring intellectual, conceptual, memory and personality dimensions.

The Wechsler Adult Intelligence Scale, a general test of intelligence, itself is comprised of many different parts each of which measures a specific function. These include General Fund of Information, Comprehension or Judgment, Problem Solving, Abstract Conceptualization, Immediate Recall of Digits (forward and back), Vocabulary, Spatial Relationships, a Symbolization or Coding Task, and subtle perceptiveness.

The Serial Seven Task which involves serially subtracting seven from one hundred and which is thought to measure mental flexibility and sustained attention was also included.

The Wechsler Memory Scale was later added because of the apparent sensitivity of the Serial Seven Task, to the battery and it measures the following functions: Personal and current information, Orientation in time and place, mental flexibility including counting backwads, reciting the alphabet, and counting forward by threes. It also tests recall for short verbal passages, visual reproduction by recall, and an Associate Learning Task.

Personality dimensions were in part measured by an objective assessment, the Minnesota Multiphasic Personality Inventory (M.M.P.I.) This test is comprised of five hundred and sixty-six self descriptive statements to which the patient responds with either a "True" or "False" mark on an answer sheet. The resulting patient Profile includes three validity as well as ten clinical scales. The validity scales include a lie scale which indicates the extent to which a patient attempts to "fake good" or "fake bad" (perhaps "social desirability" would be a good description) and an "F" Scale which measures the degree of inconsistency in the patient's answers which is thought to be a reflection of his confusion, and the "K" Scale which generally reflects test-taking attitude and/or degree of defensiveness. The Clinical Scales include such diagnostic categories as Hysteria, Depression, Hypochondriasis, Psychopathic Deviate, Psychosexual Deviate, Paranoia, Psychasthenia, (phobias, obsessiveness, compulsions), Schizophrenia, Mania, and Social Introversion.

Two projective or subjective measures of personality included the Rorschach Ink Blot Test and the Thematic Apperception Test (TAT). These tests, by the very nature of their ambiguity and lack of structure, are felt to measure underlying needs, feelings, conflicts, and in general give us some clue as to the "whys" or the dynamics of a person's personality functioning.

The Rorschach Ink Blot Test consists of ten plates on which chromatic and achromatic ink blots of a wide variety of shapes and forms are reproduced. Published norms as well as clinical experience suggest that there are "normal" types of responses indicating strengths, healthy emotional needs, personality equillibrium, etc., while at the same time there are other responses which indicate pathology of varying degrees. This pathology is seen both in terms of the type of distorted thought process the patient employs, together with the kind of bizarre content he projects to the ambiguous stimuli.

The Thematic Apperception Test (TAT) consists of a number of pictures of persons individually or in a variety of combinations all essentially in loosely structured and in a varying degree of ambiguity. Again, this looseness of structure allows for the individual patient to project his own needs onto the scene. There are a variety of scoring systems as well as clinical judgment to interpret the patient's protocol.

The Bender Visual Motor Gestalt Test was also employed. It consists of nine geometric designs which the patient is required to copy with pencil and paper. Minimal directions are employed and his approach to the task as well as content are of clinical significance. If the patient distorts the figures significantly such as in rotation or reversals, extreme difficulty in accurately reproducing angles (especially by adding additional angles) or where over simplification or elaborations are involved, then these observations together with a careful analysis of his performance on the above mentioned tests could well suggest central organic impairment.

A structured clinical interview was designed to evaluate the manner in which the patient was able to function historically prior to the onset of pain as well as currently. His description of the pain is important particularly in determining the extent to which it has or has not become a part of his life style. It was further the intent to evaluate the individual's resourcefulness, as well as the resourcefulness of the family within which the patient resides. Inquiries as to how the patient felt about possible surgery and what he hoped to gain from it was also obtained.

The information gained from the Clinical Interview together with the above tests results were carefully evaluated. If it appeared that the patient did show significant and consistent signs of organic deterioration or if it were felt that the patient was decompensating emotionally there were serious reservations as to his candidacy for surgery.

If a patient appeared depressed, confused, estranged from his family, and seemed to have the capacity for acting-out one had to consider the possibility of suicide. Additionally if the patients were depressed, anxious, confused and uncertain as to their feelings about surgery, psychiatric consultation was recommended and a decision regarding surgery was postponed.

Results:

Most of the patients who had good results from the surgical procedure did not show gross signs of intellectual, conceptual memory defect, or personality emotional deterioration. Interestingly these patients also revealed the typical "Neurotic Triad" on the M.M.P.I.: that is, elevated Hypochondriasis, Depression, and Hysteria irrespective of the origin of their pain. Patients not showing this characteristic were felt either to be in poor contact with reality to the extent that they did not realize the seriousness of what they were facing or their defective systems were screening out reality.

Comparisons between pre-surgical and post-surgical scores on the tests can only be recorded as trends at this point because of the nature of the Pilot Study with the small number of patients. As mentioned previously, the most significant trend included the elevated Neurotic Triad which almost consistently remained elevated post-surgically. The retention of this orientation is not surprising if one conceives the post-surgical patient as very cautious, self-observant, and extremely sensitive. To date we do not have an idea as to how these patients function with respect to this Triad six months to a year after surgery.

The patient's scores on the Validity Scales of the M.M.P.I. remained essentially unchanged post-surgically. However, there does seem to be one trend of questionable significance on the Clinical Scales. Post-operatively there was an increase in elevation of the Schizophrenic Scale although it should be noted that the elevations were generally not within the pathological range.

A Schizophrenic Scale includes a total of seventy-eight items which attempt to measure 1) social alienation and isolation, 2) complaints of family alienation, 3) bizarre emotions, 4) delusions, 5) somatic symptoms, 6) influence of external agents, 7) peculiar dysfunctions of the body, and 8) dissatisfaction and depression. Thus, one need not think of this patient as being necessarily more Schizophrenic — than he was prior to surgery but rather as being somewhat more confused, sensitive, and preoccupied with himself and his body functioning. Again, how persistent this trend is in time, remains a question.

In general, post-operative I.Q.'s were somewhat higher although not significantly so. It would be erroneous to conclude that the higher scores post-operatively were due to "practice effects" because of the proximity in time. Studies have shown that interpolated activities, such as surgery, between testing, has a tendency to nullify such effects.

Because the Wechsler Memory Scale was introduced relatively late in the Study there were few patients on which to make an appraisal although there seems to be a tendency toward an increase in memory function post-operatively. Again, we recognize the imposing and disrupting influence of anxiety on recall.

It was noted that there was a significant trend toward improvement post-surgically on the Serial Seven Task. Patients seemed to be able to make computations more quickly with fewer errors. This implies greater ability to attend over a protracted period of time.

The patient's post-operative responses to the Projective Personality Tests (Rorschach and TAT) tended to be greater in number and better elaborated. Thus, the patient seemed more aware and concerned about stimuli outside himself and responded accordingly. The responses were not in the direction of increased pathology either from the thought process or thought content standpoints.

The results of the patient's performance on the Bender Visual Motor Gestalt Test are essentially variable.

There were some interesting findings from the clinical interview. Post-operatively there was generally not significant change in the degree of cooperativeness. On the Aggression-Passivity continum, patients did not seem to change remarkably. It was interesting to note that on occasion the manner in which they expressed their aggressions sometimes changed. For example, patients who were formerly irritable and veiled their hostility with sarcasm and other sophisticated kinds of camouflage, sometimes post-operatively were more open or direct in the expression of these feelings. It was interesting, too, to observe with respect to their awareness of pain, most patients tended to have very definite ideas as to the success or failure of the surgical procedure after a week's time. They either felt that the pain was much less intense, that it bothered them less, or that there was little or no difference. As far as the patients' feelings about the surgery was concerned, it did not seem to depend upon their real understanding, that is, intellectual understanding about the operative procedure. Some patients who claimed to have little real understanding came out feeling very good about the surgery. Others who had great understanding about the procedure revealed disappointment. Interestingly, patients tended to be less anxious (this is a factor which may be more related to the fear of the unknown regarding the surgical procedure) following surgery although sometimes more confused and perhaps rebellious. There was some suggestion of regression in a few cases.

How effectively the patients maintain themselves post-surgically is probably related to the resourcefulness of the patient himself, resourcefulness of the family, the degree to which the patient becomes involved with his family and the outside world, and the desire to and motivation for self improvement. Many times the patient himself is in need of some type of rehabilitation in order to maximize his re-adjustment to living. This includes not only the need for possible physical rehabilitation if the patient has been relatively inactive for a period of time but also the need for psychological and social rehabilitation if the patient has been self preoccupied and socially isolated.

The Pain Clinic

In the Pain Clinic problems frequently arise where a patient has experienced pain over a sufficiently long period of time where this pain or suffering has actually become "egosyntonic," that is, a significant part of his concept of himself. It is sometimes possible to see in a detailed family history where the patient has been rewarded either directly or indirectly for his pain or suffering. This is seen not only in the patient who, for example, received gratification in the form of paternal leg massages for pain as a child and later the massages were transferred to the hands of her husband. This type of conditioning process is sometimes also seen in industrial back pain problems. After careful medical study revealed the lack of primary organic pathology and where the pain was attributed at least partly or totally to psychogenic cause, the question becomes one of how treatable the patient will be from a psychiatric standpoint. Here the psychological evaluation is designed to elaborate the individual's personality dynamics to determine just how significant a part of the person's concept of himself the pain has become and how resistant to change he is likely to be, the types of defenses he utilizes, the permeability of his defenses, the intellectual capability of the individual, the ability to form meaningful insights, intra-personal as well as inter-personal strengths, the degree of independence versus dependence, and finally, and sometimes most importantly, the desire or motivation for change or improvement. It goes without saying, of course, that again, evidence of psychotic manifestations, as well as organic impairment, as well as possible suicidal and/or homicidal risk is evaluated. On the basis of this type of study it is sometimes possible to make suggestions as to the type of psychotherapeutic program which would likely be most appropriate for any particular patient. For example, where the patient shows a need to be well or a healthy person and where he may deny pain, outpatient therapy may be the treatment of choice. However in many instances, by the time a patient is referred to the Pain Clinic his pain has become such a fixed part of his concept of himself and where his defenses are rigidly or impermeably constructed, hospitalization may be necessary in order to maximize the changes of breaking through his defenses and mustering up some motivation for change to a healthier style of life.

The contribution that the psychological evaluation has made in the overall medical handling of Cingulumotomy patients is, at this point, obviously quite modest. Yet it does point to some trends which we intend to pursue and further evaluate. It does suggest that perhaps psychological and psychiatric factors are often over looked in determining candidacy for other surgical procedures.

The psychologist's participation in the Pain Clinic is a new and challenging experience as I presume it must be for the other members. The multi-disciplined approach toward evaluation of pain cannot help but contribute to a broader understanding of all the Pain Clinic members toward these symptoms and certainly toward a better understanding of an individual patient's problems. The flexible orientation of the Staff toward evaluating these patients together with the challenge they present make participation extremely rewarding.

NEUROLYTIC BLOCKS IN THE MANAGEMENT OF PAIN

WILLIAM A. MATHEWS, M.D.

Conceptual Aspects of Pain

We usually assume that pain is a symptom of an underlying disease process and in most instances elucidation of the disease process and its proper treatment eliminate the pain. In many cases the underlying disease process is untreatable, incurable, or cannot be clearly delineated. In these cases pain assumes the role of a disease and a complete knowledge of the anatomy and physiology involved and a conceptual model of the pain process are necessary. Most of us were taught that there are specific pain receptors which transmit "pain" along pain tracts to "pain centers" in the thalamus and cortex. This concept can be mentally clarified by a look at Fig. 1 taken from the work of Casey and Melzack.[1] The problem with this concept is that it psychologically implies that the pain experience is due to one specific receptor, pathway, or center. This concept implies a "man in the brain" who senses pain, evaluates it, and decides on an appropriate response.

As one sees the pain problems that filter down to a multidisciplinary pain clinic it readily becomes obvious that we just can not effectively evaluate and treat pain this way, or if we do the failure rate will be dismally high. How can we explain the soldiers with massive wounds who feel no pain? Is it acceptable to say they are so overjoyed at being alive that they do not react to their pain? How can pain be painless? It would be much more logical to say that the sensory input was blocked or modulated by cognitive activities before it could evolve affective and aversive responses. The gate control theory of pain[2] provides a framework in which we can more effectively deal with and understand pain problems. It can be summarized by reference to Fig. 2 taken from the work of Casey and Melzak[1] without citing the anatomic and physiologic evidence the theory proposes that a "gate control system" in the spinal cord modulates the amount of input transmitted from peripheral fibers to the first central transmission (T) cells, which project to the ascending fibers of the anterolateral cord. The numbers of firings of T cells to the higher areas of the central nervous system in unit time is determined by the ratio of large to small fiber inputs and also by descending influences mediated by central-control efferent fibers. The output of the T cells is monitored centrally and over a physiologic time base triggers the action systems to elucidate the whole complex tapestry of pain in its aversive, reactional, and vegetative components.

Bonica[3] has pointed out the somatic and visceral responses to noxious stimuli many years ago. He pointed out that noxious stimuli, whether due to injury, disease, or surgical trauma, involve typical reaction patterns which are the body's method of adaption often harmful to the organism. These are:

(1) Local tissue reaction manifested by hyperesthesia, hyperalgesia, and signs of inflammation and tenderness.

(2) Reaction at the segmental levels of the cord consisting of muscle spasms, vasospasm, and alterations of visceral motor function.

(3) Suprasegmental reactions involving circulation, respiration, and autonomic centers.

(4) The integration and central interpretation of the original sensation is by definition pain and all of these complex physiologic and psychologic responses are reactions to pain. In a recent study by Bromage[4] he has clearly shown

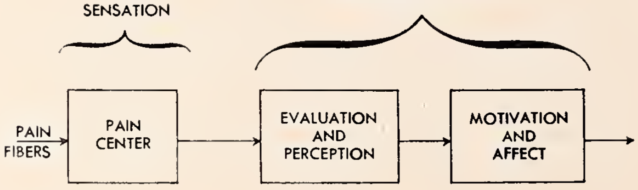

Figure 1
The older conceptual model of pain. Taken from Casey, K. L. and Melzack, R. Neural Mechanisms of Pain: A Conceptual Model. From New Concepts in Pain and its Clinical Management. Ed. E. Leong Way. F. A. Davis & Co. Philadelphia 1967.

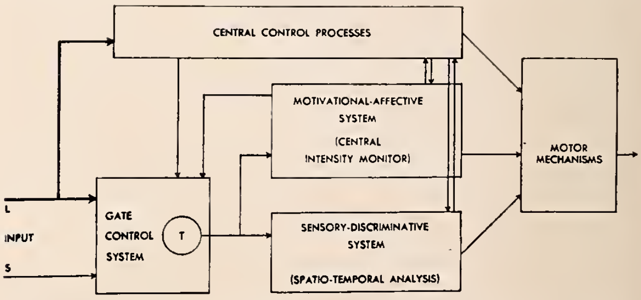
CENTRAL CONTROL PROCESSES
MOTIVATIONAL-AFFECTIVE SYSTEM (CENTRAL INTENSITY MONITOR)
MOTOR MECHANISMS
L
INPUT
S
GATE CONTROL SYSTEM
T
SENSORY-DISCRIMINATIVE SYSTEM (SPATIO-TEMPORAL ANALYSIS)

Figure 2
The gate control theory of Pain. Also taken from Casey and Melzack.

the advantages of continuous lumbar epidural analgesia for postoperative pain relief in contrast to centrally acting analgesics. These are summarized in Table 1. These are pointed out to show the physiological superiority of nerve block and neurosurgical procedures to narcotic analgesics in the management of moderate to severe pain.

Table I

Function	Change with pain	Restoration toward normal Systemic analygesia	 Epidural analgesia
Vital capacity	50-75% reduction	10-30%	70-100%
F.R.C.	0-20% reduction	Noo change	Restored to normal
Peak Expratory Flow	50-80% reduction	20% restored	Restored to normal
Central venous pressures	Raised	No change	Lowered

To return for a moment to the gate control theory let us summarize then how it fits into the management of the patient with chronic, or for that fact, acute pain. For one thing, for the first time we have a neurophysiologically acceptable basis for hypnosis and suggestibility in the control of pain. For example, cortical influences of the stoic individual can be virtue of descending central control fibers "close the gate" to ascending T fiber activity. Now it has been shown that large fiber activity closes the gate and small fiber activity opens it, or in effect facilitates the upward transmission of painful stimuli. This explains why people with long standing dull aching pains of malignancy not only never accommodate but become increasingly more aware of pain. Their gate is open by a preponderance of small fiber activity and also their central responses of depression and hopelessness increase their awareness of stimuli received. The selective destruction of large fibers as occurs in diabetic or alcoholic neuropathy, leaving small fibers relatively intact, thus tends to eliminate inhibition of input by the modulating substantial gelatinosa. This means unchecked central transmission and intense pain.

There is some evidence that the unexplained neuralgias when subjected to electron-microscopic studies also show demyelination and a decreased population of large fibers. Now there is also evidence to indicate that there is normally a downward flow of tonic impulses which inhibit sensory input, thus we have an explanation for the almost untreatable peripheral pains following central nervous system lesions. There is also evidence that drugs can exert profound effects in the substantia gelatinosa, thus providing a basis for the use of analgesics, positive reassurance, psychosedatives, and nerve blocks in a holistic approach to pain control.

Technical Aspects Of Neurolytic Blocks

In our clinical practice we will not do a peripheral neurolytic block, simply because the incidence of post-injection neuritis and motor complications in our hands has been distressingly high. It is our feeling that neurolytic blocks are not for the non-specialist, or for that matter, the specialist who uses them only occasionally. The first premise for undertaking a neurolytic block is complete understanding of all the available information gained by previous examiners, in addition to a repeat pertinent history and examination by the present examiner. We are firmly convinced that there is no place for haste in the management of chronic pain and anyone not willing to devote a great deal of time to a patient should not attempt to manage his pain. In the same vein, we should not allow referring physicians to rush us ill-advisedly into neurolytic blocks. This will lead only to ill-selected procedures and poor results.

Each patient has the nature of the proposed block explained to him and the possibility and nature of complications is discussed. He is also told that a re-block is very likely. All of this is then dictated into an individual consent form for each patient which clearly states his particular block and possible complications. This is the only way to avoid misunderstanding.

With the advent of excellent electrical radiofrequency percutaneous cordotomy in our group we have modified our feelings toward neurolytic blocks so that the following is our stand. We have had excellent results with cervical subarachnoid alcohol in superior pulmonary sulcus tumors, and neck and breast lesions confined to cervical and upper thoracic dermatomes. In patients with segmental thoracic pain the results have been almost uniformly good when a peripheral pain generator can be demonstrated. In the management of upper abdominal malignancies we have done fairly well with celiac alcohol or phenol. In segmental pain of LI distribution we have done well. In bilaterally presented pelvic pain due to malignant disease and in diffuse leg pain, the results have been so poor with blocks that we no longer even try them if percutaneous cordotomy can be tolerated. Early in the years when I was working with the M. D. Anderson group using subarachnoid alcohol, we did a large number of cases with lumbosacral distribution. The incidence of fecal and urinary incontinence was about 15% In the last year all of our lumbosacral root blocks have been done with 4% phenol in glycerin prepared by the method of Maher.[5] Careful attention to dehydration of the phenol as described by Brown[6] was done.

Alcohol Blocks

Aside from the use of alcohol to inject terminal branches of sensory divisions of the trigeminal nerve which serve as trigger areas, the direct injection of the ganglion, and autonomic nerves, our use of alcohol is confined to the subarachnoid space in the cervical and thoracic areas. The use of alcohol is predicated upon its lipolytic and dehydrating actions at a nerve rootlet and upon the fact that it is hypo-baric with respect to spinal fluid. Alcohol has a specific gravity of 0.78 while spinal fluid averages 1.007. When it is slowly injected into the spinal fluid it will then tend to layer upward, and by careful positioning of the patient the desired segments can be positioned superiorly. If we now direct attention to Fig. 3, it is easy to visualize how by the use of bolsters and tilting the table that 2-3 spinal segments may be made to lie higher than the rest of the cord. The convexity of this upward curve can also be accentuated by use of "breaking" the table and use of the gallbladder rest. In addition to the aforementioned, the patient is now rolled forward into a 45° anterior tilt and secured by means of pillows in front of him and straps over him. Fig. 4 demonstrates how by this 45° anterior tilt there is a greater tendency to space the ventral roots and maintain the highest concentration of alcohol over the dorsal sensory rootlets.[7] Should the pain have bilateral representation then one has the option of doing one side at a time, or placing the patient face down and increasing the volume of alcohol used. We prefer unilateral blocks at intervals of two or three days.

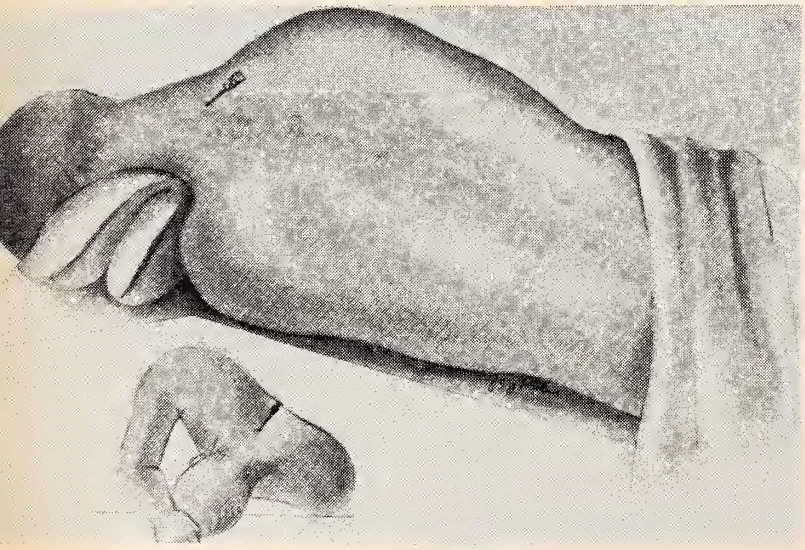

Figure 3
Method of positioning patient for cervical block with desired segment highest. From Bonica, J. J., Management of Pain. Lea and Febiger, Philadelphia, 1953.

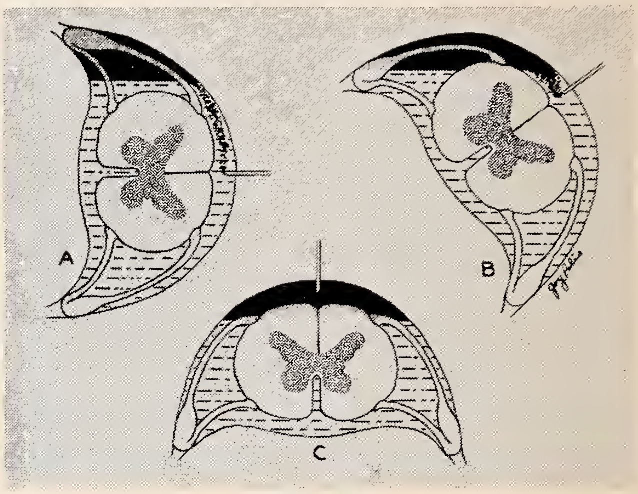

Figure 4
Showing how anterior tilt tends to layer alcohol and spare motor rootlets. From Bonica.

The careful evaluation of the segments involved by reference to standard dermatome and sclerotome charts is essential. Inasmuch as the degree of effect of a local anesthetic substance is inversely related to the square of fiber diameter it is essential for best results to place the solution opposite the fine fila radiculara of a rootlet rather than at the point of exit from the intervertebral foramina. Reference to Fig. 5 clearly demonstrates the disparity between the level of origin of rootlets from the spinal cord and the level of the vertebral body. While not exactly accurate in all patients, this diagram copied from Bonica[8] is sufficiently accurate for clinical purposes.

The spinal puncture is accomplished with a short bevel 22 gauge needle being careful to advance the needle very slowly in the thoracic and cervical regions because of the underlying cord. The amount of alcohol injected varies from the very conservative to excessive. We usually inject 0.8 to 1.0 cc. in the cervical and upper to mid-thoracic regions for each three segments desired in a unilateral block. In other words, if we are doing a unilateral block to cover T5 to T10 we would insert a needle at T6 and T9

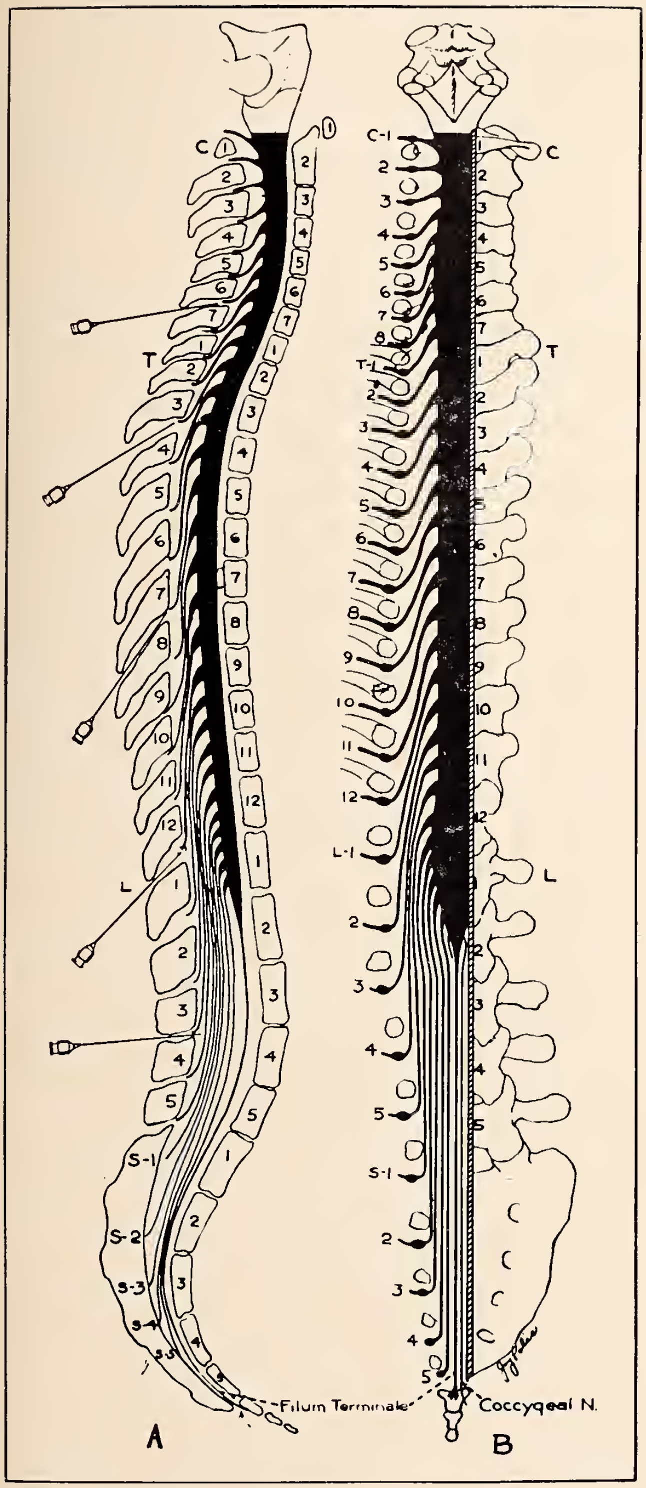

Figure 5
Demonstrating the disparity between vertebral body level and rootlet level of the cord due to spinal cord being shorter than vertebral column. From Bonica.

and inject 0.8 to 1.0 cc. at each location. This is considerably more than Bonica uses. In a bilateral block, face down, we use 1.5 cc. for each three levels, but never inject more than one level at a time.

During and within a few seconds after the injection of absolute alcohol the patient may have a sensation varying from warmth to severe burning along the course of the nerve supplied by the rootlets the alcohol has come in contact with. This is of great value in determining proper needle placement, and for this reason we do not use heavy premedications.

Following injection the blood pressure and other vital signs are observed carefully as occasionally severe hypotension will occur in debilitated patients. In our experience, the success of a block is greatly related to the ability of the anesthesiologist to maintain the patient in position for 45 minutes after the block. We will frequently give intravenous diazepam and allow the patient to sleep comfortably during this period while still monitoring the vital signs. Following this, patients are kept at bedrest 24 hours and fluids are forced. When the block is effective pain relief may occur immediately or not for several days after injection. In our experience about half of the patients with immediate relief of all their pain will have partial recurrence in a few days and have to be reblocked. The average duration of relief is three months before small fiber regeneration occurs.

We will not discuss the standard technics of blocking terminal divisions of the fifth nerve which serve as trigger points in trigeminal neuralgia.

Alcohol Celiac Plexus Block

One of the most useful neurolytic blocks in our hands has been the celiac plexus block performed with 50% alcohol. The control of the excruciating pain of pancreatic carcinoma and the pain of non-resectable or recurrent malignancies of the stomach, liver, and biliary tract have responded well. We have now used this technic in 17 upper abdominal malignancies with good results in nine, fair results in four, and poor in four. In our experience, patients who have become drug dependent will have uniformly poor results and we advocate the early use of this block.

The technic used is that of Bridenbaugh.[9] The splanchnic nerves are the principal mediators of pain arising from the pancreas, biliary system, duodenum, stomach, and small bowel. These are really visceral afferent fibers carried within the splanchnics. In this technic the patient is placed prone with a pillow under the abdomen and centered at the level of the first lumbar vertebra. The lower margin of the spinous process of T12 is found by counting upward and confirmed by counting downward, using the level of the scapular tip at T7. The superior aspect of L1 will lie at the level of the interior tip of the T12 spinous process. The celiac plexus is to be found in loose areolar tissue about a centimeter in front of this. An X is made at the spine of T12 and also at the lower edge of the twelfth rib bilaterally some 3 inches from the midline; these three points are then connected to form a triangle. The sides of the triangle will be the path followed by the needles on their way to the areolar tissue in front of the first lumbar vertebra.

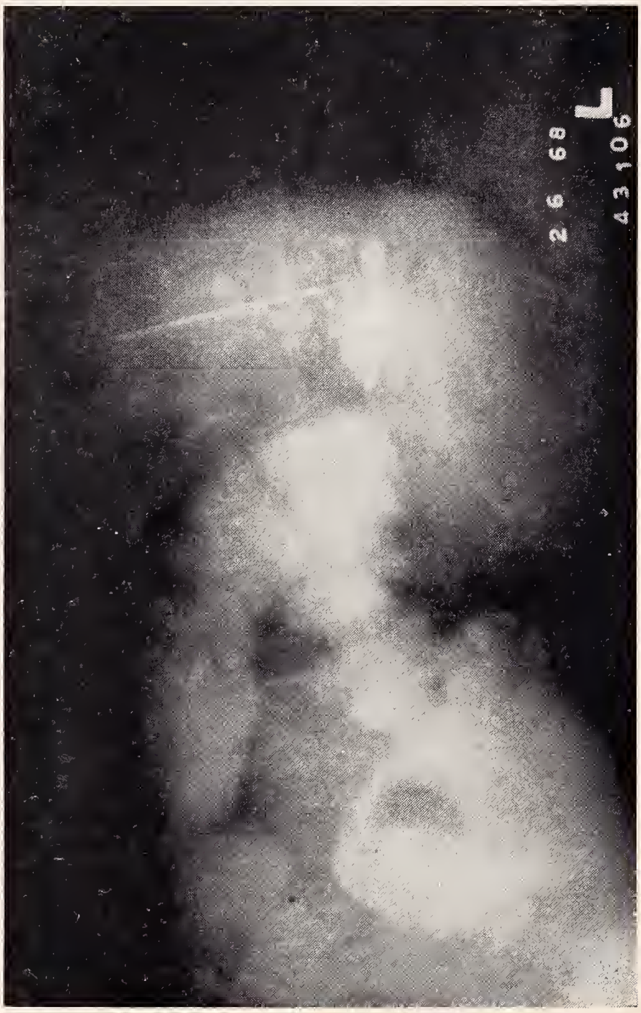

Figure 6
X-ray contrast injection showing proper needle placement for coeliac block.

We first perform the block with 25 cc. of 1.5% Xylocaine on each side, allowing an interval of 20 minutes between sides. If this produces good pain relief, the procedure is done the next day using 25 cc. of 50% alcohol on each side. We *always* confirm needle placement with bi-plane x-rays and the injection of a milliliter of contrast media. The proper placement of the needles will almost always be heralded by post-block hypotension. For this reason we have an intravenous running with a plastic needle and carefully monitor blood pressure. The average duration of pain relief from a block is three months.

Recently Copping[10] has recommended chemical splanchnicectomy at the time of operation, using 6% phenol in water. We have not used this technic but it would seem to have merit. He alludes to some animal work in his laboratory indicating more nerve fibre destruction than with alcohol.

Phenol Blocks

The use of absolute alcohol in the cervical and thoracic regions, as previously stated, has been relatively free of complications, however, such has not been the case in the lumbosacral area. The use of intrathecal phenol was initiated by Maher[11] who emphasized the decreased incidence of paresis and loss of bladder control. Several agents have been used as carrying vehicles for the phenol, namely iophendylate and glycerin. Experience with concentrations varying from 7% to 2% phenol in glycerin has led to the conclusion that the safest effective concentration is 4%. A variation on this is to combine 0.04% silver nitrate with the phenol in glycerin. Unless the glycerin is first dehydrated as described by Brown[13] excessive neurolysis will occur.

Maher[12] has previously stated that there is a sparing of large fibers with the phenol technic. Such is definitely not the case as our own limited observations and those of Smith,[13] and Baxter[14] have shown. There is destruction of all fibers with possibly a total population destruction of more small than large fibers. Both of these workers describe posterior column degeneration in about 25% of their specimens. This has been most interesting to us as we have seen severe posterior column signs in patients given 6% solutions, though there is no reference to this in any paper in the literature. The lesions at autopsy and the clinical results with iophendylate as the medium show inconsistent results so that we use only glycerin as a solvent. In contradistinction to alcohol, phenol in glycerin is hyper-baric, having a specific gravity of 1.25 in contrast to spinal fluid which averages 1.007.

The patient is placed with the affected side down and at a slight head-up tilt. Lumbar puncture is done one segment above the roots to be blocked. Puncture must be done with a 20 gauge needle or the phenol-glycerin solution will be impossible to inject. The phenol is injected very slowly in two increments as shown in Table II. The patient first notices loss of pain, then warmth, then blunting of sensation and very slight motor weakness. The patient is observed after 5 minutes and if loss to light touch with a cotton wisp or motor weakness are still present, then the second increment is not given. The phenol will settle into the dural sheathes of several roots depending upon the volume and the level of injection, as the sacral and lumbar dural sheathes are larger than the thoracic. It is much better to do multiple injections than risk complications with high volumes. The superficial abdominal reflexes and tendon reflexes disappear, but gradually the tendon reflexes return. The patient is sedated and kept in position for 45 minutes. If relief of pain persists for over two weeks, the results are usually permanent. Inasmuch as the phenol is deposited into the dural sheathes, there is not the discrepancy between vertebral level and nerve root level seen in the alcohol technic. By the same token, adhesive arachnoiditis will obliterate dural-sleeves and in this case, phenol cannot reach the roots to be of benefit.

Summary

The gate control theory of pain has been presented and its application to clinical pain problems has been suggested. The pros and cons of several different neurolytic technics which can definitely alleviate pain with minimal disability to the patient have been adumbrated. Extreme care is necessary in any neurolytic technique.

Table II
Dosage For Subarachnoid Phenol Injection

Sacral roots	0.1 + 0.1 ml. in 5 minutes
Lumbo-sacral roots	0.2 + 0.2 ml.
Mid-lumbar area	0.2 + 0.3
Thoraco-lumbar area	0.3 + 0.3

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SUMMARY

As the Seminar developed during the course of the day, and each speaker presented his facet of the pain control problem, I was reminded of the parable of the elephant described by the blind men. Interdisciplinary meetings such as this one have as their greatest value a synthesis of parallel but overlapping view points. The unfortunate individual with intractable pain is receiving increasing attention rather than being relegated to the limbo of therapeutic failures. Old ways of viewing central pain mechanisms are being replaced by new exciting view points which will serve as the foundation for the ever accelerating number of procedures available to such sufferers. An appreciation of the interaction between psyche and soma assumes great practical importance for the physician and his patient in forging the therapeutic decisions for the management of intractable pain. I feel that the prayer with which Sister Mary dePaul opened the Seminar is also appropriate in summarizing its closing.

Almighty God

We ask your blessing on all here assembled and on those who made this Seminar possible.

Equip us with inquiring minds.

Let us be comforted by the thought that we can but trust you.

Startle us with great ideas.

Help us leave our corner of the world a little better than we found it.

James R. Atkinson, M.D.

ONE LESS MONTH TO GO

This month saw two long-term endeavors of the Association come to pass. Both of these were meetings with other health groups. On October 10 & 11 a group of 30 MD's and 30 nurses met in the Velda Rose out of Mesa. It was keynoted by Dr. Barbara Bates from Rochester, New York who pointed out the present vertical chain of command between doctor, nurse and patient, with the doctor firmly at the top, and suggested that this was going to change to a more horizontal one, with both doctor and nurse responsible for a specific area of therapy. Dr. Lambretsen, of Columbia, states that some primary care in the future, would be given by nurses. With this as a start to sort of beat us down, we broke up into groups of approximately six doctors and six nurses, to discuss these and other concepts of problems. Needless to say, there wasn't complete agreement on these or some other points, but there was agreement that the nurse of the future would have more responsibility in patient care. There was also agreement that all diploma schools would soon be closed and all nursing personnel would come from educational institutions, university, college and technical high school. Dr. Payne's committee will give a complete report on this in the near future.

On October 25th, the Executive Committee of ArMA and the Executive Staff met with a like group from the Arizona Osteopathic Association. We found we had some mutual problems in our inability to control some of our members. A recent look at the papers will show this quite clearly. This publicity, however, usually only states "doctor" and all doctors in the state suffer a bit. The osteopaths also have a malpractice problem and feel that doctors in general are getting bad press regarding abuses, increases of fees and increasing cost of particularly the Medicare program. It was felt that this sort of liaison committee was worthwhile and tentatively it was planned on having two such meetings a year. It was also felt, particularly in the legislative field, that our two organizations could accomplish by working together what neither one of us could accomplish by ourselves.

It would seem that the days of the absolute ruler are indeed numbered.

Dean's Page

CHANGING PERSPECTIVES IN MEDICINE

Many of us have lost sight of the fact that in the pre-Flexner era, there were two characteristics of medical education which have disappeared from the contemporary scene. First, because medical education was generally preceptorial, each new physician was essentially a replication of his tutor; and second, the system operated in such a way that almost any interested student could be admitted to the study of medicine, as long as he could afford it.

After 1910, and the Flexner Report, medical education moved to the campus of the university and assumed a new aura of respectability as a consequence of the underpinning it received from the addition of the basic sciences. The influence of the university and the interposition of the basic sciences between undergraduate work and clinical medicine combined in such a way as to produce two new characteristics within our system of medical education; characteristics which may yet prove to be quite as undesirable as those that were displaced. First, the enormous competence of medical school faculties tends to result in the production of a physician who is probably overtrained relative to the actual needs of the society he serves; second, the scientific structure that undergirds contemporary medical education has proven to be unexpectedly rigid and constitutes a bottleneck through which we have been absolutely unable to move a sufficient number of new physicians.

It has been estimated that most doctors will practice for about forty years. Thus, most of the physicians who were trained in the pre-Flexner ear were disappearing from the American scene as we approached World War II. The "bottleneck" effect of the Flexner Report kept us from staying even with this loss and, when superimposed on the continued growth of our population, resulted in a physician shortage after the Second World War. A small number of new medical schools were started at about that time but they could not compensate for the ebbing physician population and, as a consequence, the shortage got worse. Finally, within the current decade, we have adopted a major shift in our public policy by agreeing that access to good health care should be considered a right of all citizens. Soon afterwards, Federal legislation was passed to implement this policy. The effect of this legislation was to highlight the manpower shortage even further.

Fortunately, there has been a partial compensatory response. The Health Professions Educational Assistance Act was passed in 1963 and, as a consequence, approximately 20 new medical schools have since been activated or approved for activation. More important, many of the older medical schools have agreed to respond to the physician shortage by expanding their enrollments.

Although this response is a source of reassurance to many of us, there is some reason to believe that it cannot solve the problem because, in the final analysis, it fails to treat the two characteristics of the post-Flexner era mentioned above: the phenomenon of overtraining and the bottleneck imposed by the scientific underpinning of the medical curriculum. The new medical schools are, to all intents and purposes, simply replications of those now in existence and, as a result, they cannot be expected to do much more than to provide a partial correction of the deficit in numbers.

It seems clear that two things must inevitably happen within this decade. First, because medical schools are overtraining relative to the greatest needs of our society, a new professional will undoubtedly make his appearance; one who is better suited to meet the more immediate needs of our people. Second, since the financial support of medical education has recently escalated to a very high level, our society is soon going to insist that a career in medicine be available to all applicants who are reasonably qualified. Meeting these objectives will bring us full circle, with respect to Flexner, and watching the medical schools as they try to come to grips with these two questions is going to be interesting indeed.

Monte DuVal

AESTHETICS

THE WINE AND BREAD OF THE SOUL

WILLIAM B. McGRATH, M.D.

One of our editorials, "Latency Period," got us embroiled in the controversy over sex education. This was inadvertent: the sex issue seemed of secondary significance, a shibboleth, in the context of thoughts which were en route to explication.

The study of mores and morality should be subsumed under the general subject of aesthetics. This is the branch of philosophy which ought to be formalized and brought into the grade schools and systematically unfolded at each successive level of learning.

Aesthetics is not being taught as it should be, as a subject at least as essential as reading or mathematics. There are classes in appreciation of music and art, it is true, but they are considered of small concern and they come too late. The subject is otherwise presented in piecemeal fashion or practically ignored. The vicious circle is such that there are fewer and fewer individuals who will be qualified to teach it.

What a very worthwhile task it would be for a group of experts to outline an entire course in aesthetics: the general principles and the specific applications appropriate to each grade level, on into university and adult education.

It is a pleasant subject, aesthetics, and perhaps this is why we are disposed to pass it over without pausing to understand its sublime importance. For other kinds of ignorance there may be some excuse. But not to know or care about the evaluation of quality, not to cultivate good taste, is to be both impoverished and ignoble.

The subject has appeal and immeasurable value for young people. They enjoy learning to discriminate, learning to see the difference between the genuine and the counterfeit. They want only to know the criteria of judgment.

One can start anywhere: the rag content of good paper; the simple arithmetic of a musical chord or the measured rhythm of a verse or song; the properties of an excellent illustration in a story-book.

A child will be quickly pleased to find out why this shirt or that dress, by virtue of its fabric and stitching and tailoring, is of desirable quality or is not. A boy will be glad to be shown how to recognize superior workmanship and material in anything from a pair of shoes to a cabinet to a record player. It should be pointed out to a youngster why this piece of furniture or that place-setting is attractive and in good taste.

Every lad fancies himself an expert on automobiles. He can be made patronizingly aware that garish chrome and puerile insignia (XL 500, Mark 8, 499-SS) are insulting his intelligence because they add nothing to the functional value of a car.

From an attentive, constructive criticism of snap-shots and photographs, one can move on with steady progress to teach how to judge the merit of a movie or a television program.

Millions of poor, masochistic people have never been told that valid principles of criticism even exist!

In these days the human mind desperately needs some defense against things that are cheap or indecent and people who are ill-bred and vile. The problems of the poor, for example, will not begin to be solved by providing more food and clothing and money. A stroll through the slums will expose their desolate disregard of beauty.

The poor in fact are poor in spirit. They will tolerate unnecessary ugliness, ugliness not just in their physical surroundings but even in the most intimate aspects of their lives. All the hideousness of poverty is spreading by invitation or default. Look at any thoroughfare with its billboards and service stations and hamburger stands. The neighborhoods and private dwellings of the rich are becoming like small fortresses, trying to wall out the desecration of our environment. But higher walls and stronger shutters will not protect one's home from befoulment by certain television comedians and a lot of offensive commercials.

There are several obvious reasons for the epidemic spread of ugliness. Avarice is one. The amusement industry and the advertisers will flaunt whatever shocking vulgarity it takes to get attention. Secondly, the quantitative aspect of assembly line production lends itself to the lowest possible standards of quality and taste. Lastly, our concepts of democratization and social equality are hypocritical and unhealthy. Some people, even including professors and politicians and clergymen, seem to find some sort of spurious pride or virtue in the pursuit of commonness. Maybe, as a matter of fact, they do not know any better.

People are influenced by their surroundings. No; they are fashioned and molded and cast by their surroundings. The spiritual environment; the landscaping and architecture and interior design; music and dancing and art; elegance in manner and speech; — all these, but also awareness of fine quality in anything you can name, — these are the wine and bread of the soul.

Between beauty and goodness there is an inseparable bond. This has been affirmed by classical philosophers and always, of course, by poets. (Modernize the rituals of the church? As well "modernize" Beethoven or Rembrandt!) An individual can be taught from an early age to appreciate beauty — and then to demand it in everything about him. When he has learned the methods and standards of judging, and how important it is to judge, then he will more happily turn away from any sordid relationship or any dishonorable situation.

Topics Of Current Medical Interest

THERAPEUTIC ABORTION

The Arizona Medical Association has passed resolutions each year for three years favoring a change in the law on therapeutic abortion in Arizona. Because of this, physicians have been asked by patients and others to explain why a change is desirable and in what way the law would be altered. The purpose of this article is to provide the physicians and surgeons of Arizona with clear answers to the questions commonly asked about this issue.

Arizona does have a law on therapeutic abortion. It states that a therapeutic abortion can be performed only to save the life of the pregnant woman. A large majority of the Arizona medical profession feel that this law is too restrictive, that it ignores several well established medical indications in which a therapeutic abortion may be justified. These additional indications include: pregnancies which result from rape or incest; pregnancies which present a substantial risk of serious impairment to the physical or mental health of the woman; pregnancies in which there is a substantial risk that the child would be born with serious physical or mental defect. These additional indications have been included in almost all of the laws of several other states which have changed and updated their statutes since 1967.

Why The Law Should Be Changed

In February, 1969, The Arizona Medical Association Foundation released the results of a poll conducted in Arizona on "Attitudes Toward A Legalized Abortion Law In Arizona." This showed that 67% of the people of Arizona favor liberalizing the existing Arizona abortion law. With a large majority of both the people and the medical profession feeling that the present law is no longer realistic, both groups are placed in untenable positions. Women who feel that an induced abortion is needed and who fall within the above expanded indications are either forced outside the law to obtain an abortion in an expensive and often dangerous and degrading way, or they must travel to other countries where abortion has been legalized. It is not surprising that they resent this situation and often develop a misdirected animosity toward the medical profession for making these unsatisfactory alternatives necessary.

Physicians, too, face the dilemma of not being able to practice medicine according to their best judgment, or of going outside the law to advise or perform a therapeutic abortion, risking legal involvement which could result in the loss of their license to practice medicine. Few physicians would take such a risk.

The recent California Supreme Court decision which ruled the 1850 California law on therapeutic abortion to be unconstitutional under the 14th amendment, an invasion of privacy, could be important in Arizona. Our present law is almost identical to the 1850 California statute. The full impact of such a decision will not be felt until the U.S. Supreme Court rules on such a case. (This is not likely in the California decision as this state no longer operates under that law.) However, the implications are interesting and should spur the Arizona legislature to consider with even greater attention the advisability of changing our existing law.

How The Law Should Be Changed

There are two differing ways in which the present therapeutic abortion law could be changed. The first is to follow the lead of the other states and enact a law to allow therapeutic abortions in the expanded indications listed earlier (rape, incest, to preserve the physical and mental health of the mother, and to prevent serious physical or mental defect in the child.) The second way is to leave all decisions on therapeutic abortions to the combined judgment of the parents, physicians and hospital as it is in other medical problems. The Ad Hoc Committee On Revision Of The Therapeutic Abortion Law has considered both approaches carefully and has decided to work toward the first view. The political climate in the legislature seems to dictate this approach. This committee, together with the Arizona Medical Association Legislative Committee, will attempt to work closely with the legislature in its next general session beginning in January, 1970.

In conclusion, let me say that I know of no physician in Arizona who desires to perform more therapeutic abortions. It is an unpleasant task which in certain circumstances must be done if we are to serve the best interests of our patients. Those who strongly oppose reform in this area should take comfort from the fact that no legislation will ever be encouraged by any group representing the Arizona Medical Association which would require any woman to submit to an abortion or any physician to perform an abortion against his moral, religious or professional judgement.

William E. Davis, M.D.
Chairman
AD HOC COMMITTEE ON REVISION OF THE THERAPEUTIC ABORTION LAW

BOARD OF MEDICAL EXAMINERS

The following doctors of medicine were issued licenses to practice medicine in the State of Arizona, on October 11, 1969:

5505 ACCARDI, Vincent (GS), 312 A E. Hill Ave., Gallup, New Mexico
5506 ANDREW, William F. (OTO), 2865 Atlantic, Long Beach, California
5507 ANSCHUETZ, Robert (GS), 200 W. Third Street, Alton, Illinois
5508 BEEMAN, Joseph A. (FOP), 9010 N. Shadow Mountain Dr., Tucson, Arizona
5453 BENDING, Glenville C. (OPH), 2020 N. Waterman St., San Bernardino, Calif.
5509 BINDER, Morris (IM), 5818 Dempster Street, Morton Grove, Illinois
5454 BLOEMKER, Ernst F. (OPH), 7661 N. Harcourt Rd., Indianapolis, Ind.
5455 BOGOST, Bruce R. (P), 944 N. Sleepy Hollow Lane, Milwaukee, Wisc.
5456 BOHNERT, William W. (U), 1100 W. Michigan St., Indianapolis, Ind.
5457 BRINKMAN, John H. (IM), 116 N. Washington, Mason City, Iowa
5510 CAMMER, Leonard (P), 110 E. 82nd Street, New York, New York
5458 CAMPBELL, James E. (P), 3819 Elston Ave., Chicago, Illinois
5459 CANNELL, Robert C. (GP-PD), Marine Air Corps Sta., Yuma, Arizona
5460 CHRISTIAN, Charles D. (OBG), Coll. of Med., UofA, Tucson, Arizona
5511 CLARK, Edith L. S. (P), 50 North Medical Dr., Salt Lake City, Utah
5461 COHEN, Donald B. (IM), 4801 Church St., Skokie, Illinois
5512 CURD, Jr., George W. (IM), Veterans Adm. Hospital, Phoenix, Arizona
5513 DEWEY, Louis S. (GP-OM), 750 Swift St., Richland, Washington
5462 DIENER, Carl F. (IM-PUD), Coll. of Med., UofA, Tucson, Arizona
5463 DOCTOR, LeRoy (IM), 4801 Church St., Skokie, Illinois
5464 DUPONT, Joseph A. (ORS), 103 Tarpon, Galveston, Texas
5514 EDIDIN, Bernard (IM), 4801 Church St., Skokie, Illinois
5465 EHRLICH, Morton E. (U), 512 University Towers, El Paso, Texas
5466 FULGINITI, Vincent A. (PD), Coll. of Med., UofA, Tucson, Arizona
5515 FURR,JR., Walter Eugene (GS), 600 E. 25 Street, Hialeah, Florida
5467 GEE, Franklin (GP), 21 Area Dispensary, Camp Pendleton, California
5468 GOODKIN, Robert (NS), 4 Peter Cooper Rd., New York, New York
5516 GOODRICH, JR., Frederick W. (OBG), 1825 E. Roosevelt St., Phoenix, Ariz.
5469 GUSTASON, Gary A. (OPH), 2225 Acorn Road, St. Paul, Minnesota
5544 HAN, Sang Yeung (R), Univ. of Alabama Med. Ctr., Birmingham, Alabama
5470 HANTMAN, Stephen L. (IM), 1125 Graham Rd., Florissant, Missouri
5471 HARVEY, Meldrum J. (GP), P. O. Box 1729, Lake Havasu City, Arizona

5517 HEINZERLING, Carl R. (GP), Doctors Park, Chaska, Minnesota

5518 HIRSCHBERG, J. Cotter (P), Menninger Foundation, Topeka, Kansas

5519 HOBBS, Elmer T. (GP), 6500 Holdrege, Lincoln, Nebraska

5472 HOLLANDER, Arnold I. (IM), 1832 S. Camino Seco, Tucson, Arizona

5473 HORNICK, Frederick W. (OBG), Maricopa Co. Gen. Hosp., Phoenix, Arizona

5520 HOUCK, John H. (P), 200 Retreat Avenue, Hartford, Connecticut

5474 INGRISH, Frank (D), Naval Air Station Hosp., Jacksonville, Florida

5521 JACQUES, Raymond B. (OM-GS), 13430 N. Black Canyon Hwy., Phoenix, Arizona

5475 JAMISON, John B. (R), 417 Church St., #34, Galveston, Texas

5476 JONES, William A. (GPM-AM), 3370 Miraloma Ave., Anaheim, California

5477 JORGENSEN, Roger L. (OPH), 1350 Tulip St., Longmont, Colorado

5522 KELTY, Richard H. (IM), 2613 W. Tuscarawas St., Canton, Ohio

5523 KOENIGSBERG, Noah M. (IM), Arizona State Hosp., Phoenix, Arizona

5524 KUHE, Emil B. (GS), 9839 – 103rd Ave., Sun City, Arizona

5478 KUIVINEN, Ned A. (PATH), 550 W. Thomas Road, Phoenix, Arizona

5525 LAIRD, JR., Frank W. (ANES), Maricopa Co. Gen. Hosp., Phoenix, Arizona

5479 LEE, Leslie H. (GS), Veterans Adm. Hospital, Phoenix, Arizona

5480 LEVENSON, Alan I. (P), Coll. of Med., UofA, Tucson, Arizona

5481 LEVY, Norman S. (OPH), 950 E. 59th Street, Chicago, Illinois

5526 LEWIN, Isaac (IM), 4402 E. Broadway, Tucson, Arizona

5482 LYONS, Irwin (P-CHP), 223-C Benson East Apts., Jenkintown, Pennsylvania

5483 McCORKLE, Marilyn R. (GP), 1461 E. Third St., Mesa, Arizona

5528 McGREEVEY, John F. (R), 1400 Todd Ave., N.W., Warren, Ohio

5484 MacDONALD, JR., James M. (GP), 888 S. King St., Honolulu, Hawaii

5529 MacNEAL, John A. (GP-GS), 379 S. Broad, Hillsdale, Michigan

5485 MENRELSSOMN, Alan N. (CRS), 3535 W. 13 Mile Rd., Royal Oak, Michigan

5486 MENENDEZ, Moran (P), Arizona State Hospital, Phoenix, Arizona

5487 MERKLING, JR., Fred C. (P-N), Arizona State Hosp., Phoenix, Arizona

5488 MILLER, Stuart (D), USAF Regional Hosp., Davis Monthan AFB, Tucson, Ariz.

5489 MONHEIT, Peter I. (GP), USAF Reg. Hosp., Davis Monthan AFB, Tucson, Ariz.

5530 MORGAN, William L. (ANES), 1417 – 15th, Longview, Washington

5490 MORSE, James O. (IM), Veterans Adm. Hospital, Tucson, Arizona

5541 MYHRE, James G. (IM), 4620 Roanoke Rd., Minneapolis, Minnesota

5491 NELSON, Donald R. E. (OBG), 1836 N. 122nd St., Wauwatosa, Wisconsin

5492 OGDEN, David A. (IM), Veterans Adm. Hospital, Tucson, Arizona

5493 O'ROURKE, Robert A. (IM-CD), Coll. of Med., UofA, Tucson, Arizona

5532 PICOTTE, Lyman W. (GP), 600 Bay Strete, Chippewa Falls, Wisconsin

5533 POMEROY, Thomas C. (TR), 5102 W. Campbell Ave., Phoenix, Arizona

5494 RAPPOPORT, William J. (CD), 2045 Franklin St., Denver, Colorado

5495 RAVENHOLT, Otto H. (PH), 625 Shadow Lane, Las Vegas, Nevada

5534 RENO, Edward C. (ANES), 8120 E. Whitton, Scottsdale, Arizona

5496 ROBERGE, Jerome T. (U), 440 – 24th St., Yuma, Arizona

5535 ROBINSON, Milton I. (GP), Arizona Children's Colony, Coolidge, Arizona

5497 ROMMEL, Frank L. (PM), 119 Larchfield Dr., McKeesport, Pennsylvania

5498 RUCKER, Charles M. (GS-TS), 550 W. Thomas Road, Phoenix, Arizona

5536 SCHWIMMER, Julius (IM), 121 East 60th St., New York, New York

5499 SECRIST, JR., Delbert L. (CHP), 8538 Larkdale Rd., San Gabriel, Calif.

5537 SHEHAN, Thomas A. (GP-GS), 30539 Pinetree Road, Pepper Pike, Ohio

5538 SILVERSTEIN, Martin E. (GS), 671 Second Ave., New York, New York

5539 STEIN, Samuel (P-N), 4535 Oakton St., Skokie, Illinois

5500 SZUTER, Carl F. (OPH), 1550 E. Indian School Rd., Phoenix, Arizona

5501 TALARICO, Leonard (U), 26 S. Goodman St., Rochester, New York

5540 TRIER, William C. (PS), Coll. of Med., UofA, Tucson, Arizona

5545 von POHLE, Charles E. (GP), 25 W. University Dr., Tempe, Arizona

5541 WEEKS, George R. (ANES), 937 Broadway, Cape Giradeau, Missouri

5502 WEINER, Gerald H. (ORS), 303-A 1st Federal Plaza, New Castle, Pennsylvania

5503 WEST, John R. (D), 251 Cajon St., Redlands, California

5542 WILSON, J. Allen (IM), Veterans Adm. Hospital, Tucson, Arizona

5546 WINDLER, Gerald (P), Veterans Adm. Hospital, Sepulveda, California

5504 WISNER, Harry K. (PS), Univ. of Texas Med. Branch, Galveston, Texas

5543 ZUKOSKI, III, Charles F. (GS), Coll. of Med., UofA, Tucson, Arizona

The following doctors of medicine are practicing under Temporary Licenses as indicated:

1291 BAKER, Leonard R. (PD), Ganado, Arizona 2/14/70

1263 BEVANS, JR., David W. (GP), Arizona State Hospital (Renewal) 11/21/69

1290 BILLINGS, Anthony C. (GP), St. Luke's Hospital 2/11/70

1298 Di CELLO, JR., Michael A. (GP), Chandler, Arizona 3/2/70

1271 DOOLEY, James H. (GP), Superior, Arizona 1/7/70

1268 FLOREZ, Jaime (OTO), Douglas, Arizona 1/1/70

1294 FREY, Charles T. (GP), Ganado, Arizona 2/22/70

1286 GOLDEN, Archie S. (PD), Ganado, Arizona 1/30/70

1269 HAMILTON, Longstreet C. (R), Flagstaff, Arizona 1/1/70

1306 HARVEY, Thomas G. (GP), Ajo, Arizona 4/15/70

1299 KIRKLEY, William H. (OBG), Ganado, Arizona 3/4/70

1265 LARSON, Oliver E. H. (GP), Ganado, Arizona 12/15/69

1303 LOESCHER, Albert (GP), Willcox, Arizona 3/26/70

1304 MANWELL, Claire C. (PD), Ganado, Arizona 4/1/70

1300 MANWELL, Edward J. (GS), Ganado, Arizona 3/4/70

1292 MEYER, JR., Alfred C. (GS), Ganado, Arizona 2/14/70

1264 PARSONS, Robert L. (IM), Ganado, Arizona 12/1/69

1285 PUTCHA, S. M. (ORS), Sierra Vista, Arizona 1/23/70

1293 REICHENBERGER, Jerome C. (IM), Sun City, Arizona 2/14/70

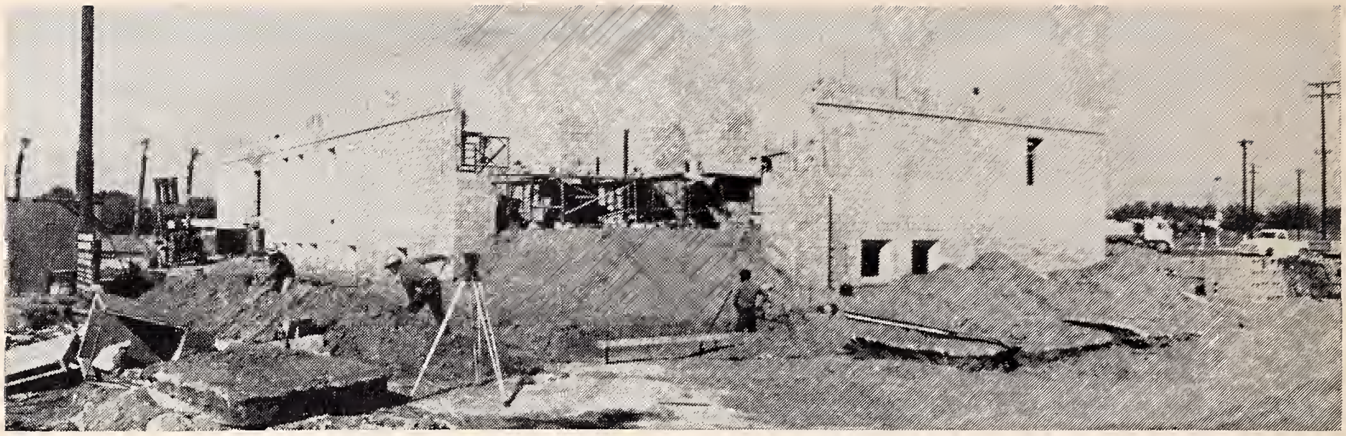
1283 ROSAS, William J. (U), Yuma, Arizona 1/15/70

1301 SINGSEN, Bernhard H. (PD), Ganado, Arizona 3/4/70

1302 WASKI, Albert T. (GP), Williams, Arizona 3/25/70

1307 DAVIE, Victor V. (GP), Morenci, Arizona 5/3/70

1308 STEINER, Nicholas (IM), Maricopa Co. Gen. Hosp., Phoenix, Arizona 5/3/70



HEADQUARTERS BUILDING REPORT

Well, it's up! Yes, the walls and huge entranceway pilasters are all completed and the masons are through. It is going to be a very striking and imposing edifice.

The entire first floor (semi-basement) for future expansion is complete and the amount of space provided is startling. We should have ample area there to take care of our needs for the next twenty or twenty-five years. Of course, the corner to be occupied by the air conditioning unit is not yet complete, but the installation of that equipment could begin anytime now.

Roofing will be the next phase of construction and this should be completed shortly. Perhaps by the time this report is published and distributed the roof, windows and doors will be in place and the building ready for interior work. That phase will of course be the interesting part as we see the rooms and various departments take shape and be compelted. We will keep you posted.

And now about finances: to date 807 doctors have paid their $125.00 assessment. An additional 600 have paid one or two installments toward their ten year program to total $150.00. This leaves us with a sum of $166,924.78 already collected and available to pay the building costs. The balance will have to be borrowed from a local financing institution, and, at the high rate of interest currently required, the eventual cost of our headquarters will rise sharply. Therefore, any of you who are able to pay the balance of your assessment this year or in 1970, should try to do so. If you will, the cost of borrowing can be cut way down and possibly be eliminated. As we are still in the year of the surtax, now would be an excellent time to take that extra deduction on your tax statement. As your accountant — this may be the best time for you to complete your assessment.

Robert A. Price, M.D., Chairman
Ad hoc Building Committee

ROBERT D. RAWSON, M.D.

1925-1969

When Bob Rawson loaned me Gerald Greene's *The Last Angry Man,* I was immediately struck by the similarities and the differences between him and the hero of the piece.

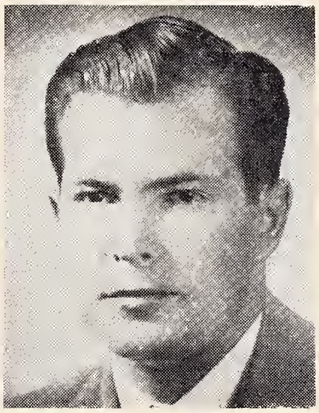
Both started, small in stature, as gymnasts. Bob starred at Southern Illinois University and thrilled the spectators between the halves of the basketball game there. He later startled the patrons of Tucson Medical Center's Donor Dinner Show with his artistry on the trampoline.

Both were dissatisfied with the state of society and medicine, but whereas Greene's character showed his pique to his patients, family and friends, Bob showed his by speaking out with conviction at surgical committee and staff functions, sometimes alone and ill-heeded. Later, after the heat of controversy had subsided, even his antagonists would amiably concede, realizing that Bob had spoken from thought and conviction rather than from emotion.

Both men loved nature, but rather than being content with a well-tended garden in New York's teeming slums, Bob had all outdoors. He studied astronomy through his telescope so carefully constructed by him in quiet moments. Much of his knowledge of the skies stemmed from his experience as a pilot in World War II. He knew intimately the glories of the Grand Canyon and the Kaibab Forest. He didn't wring his hands about the declining state of our Wild Areas, but rather became an active, participating member of the Sierra Club, Pima Conservation Council, National Parks Association, National Wildlife Association and, as a representative of "Arizonans for Water Without Waste," went to Washington to testify before the Senate Committee hearings on water conservation, thereby adding his strength to the preservation of the Grand Canyon free of dams.

Greene's character had the talent and the desire for life as a surgeon but never achieved it. Bob, backed by his wife, Kim's, strength and determination went instead to certification by the American Board and became one of Tucson's fine surgeons.

Bob's sudden death on June 13, 1969 left his wife and five children with a legacy of integrity, social responsibility, love of nature, music and man. He was an "angry young man," but not of Gerald Greene's type. Those who knew him now must carry our legacy with his intelligence, strength and determination. W. A. Soland, M.D.



JAMES W. DAVIS, M.D.

1920-1969

Doctor James Wilson Davis, son of Doctor W. Claude Davis and Ximena K. Davis, was born in Bellefontaine, Ohio on September 2, 1920. He, with his family, came to Tucson, Arizona in 1927.

He was graduated from Tucson High School in 1937 and the University of Arizona in 1941. His medical degree was obtained at Washington University in 1944. He went to active Navy duty immediately following graduation. He was discharged in 1946 and returned to Tucson and active practice with his father.

While in Medical College, he married a school sweetheart, Marjorie Peterson. Three children were born to them; Jame— age 22, Michael— age 17, Catherin— age 16. All of whom survive.

Both Dr. Jim and his brother Dr. William E. Davis were recalled to active service throughout the Korean conflict and after their discharges, both joined their father in practice until Dr. Jim's death on September 3, 1969.

Dr. Jim was a member of the American Medical Assn., Arizona Medical Association and Pima County Medical Society. He was director of the American Red Cross blood bank in Tucson from 1954 to 1957.

ARIZONA HEART ASSOCIATION

THIRTEENTH ANNUAL CARDIAC SYMPOSIUM

Biltmore Hotel — Phoenix

Friday, Saturday & Sunday, January 16-18, 1970

FRIDAY, JANUARY 16, 1970

8:15- 9:00	Registration in the Lobby
9:00- 9:05	Greetings — Auditorium
9:05- 9:50	"Indications for Electrical Pacing (temporary and permanent) and Types of Pacemaker Generators, Sites of Insertion, Unipolar Versus Bipolar" — Dr. Furman
9:50-10:35	"Testing of Pacemaker Function after Implantation and Complications of Electrical Pacing of the Heart" — Dr. Sowton
10:35-11:00	Coffee Break
11:00-11:45	"Wada Hingeless Valve and Knotless Suture Method for Fixation" — Dr. Wada
11:45-12:15	Question and Answer Period — Guest Speakers Participating
12:15- 2:00	Lunch
2:00- 2:45	"Non-invasive Methods of Measurement of Cardiac Function" — Dr. Weissler
2:45- 4:00	Panel Discussion of Presentations Guest Speakers Participating — Dr. Ewy — Moderator

SATURDAY, JANUARY 17, 1970

8:15- 9:00	Registration
9:00- 9:05	Greetings — Grand Ballroom
9:05- 9:50	"Preservation Methods of the Honor Heart" — Dr. Wada
9:50-1035	"Results of Investigation of Patients with Angina by Exercising Tests and Atrial Pacing" — Dr. Sowton
10:35-11:00	Coffee Break
11:00-11:45	"The Heart in Heart Failure" — Dr. Weissler
11:45-12:15	Question and Answer Period — Guest Speakers Participating
12:15- 2:00	Lunch
2:00- 2:45	"Interpretation of Pacemaker Electrocardiograms" — Dr. Furman
2:45- 3:15	"Uses of Newer Agents in Management of Arrhythmias and Angina" — Dr. Sowton
3:15- 3:45	Coffee Break
3:45- 5:00	Panel Discussion — Guest Speakers Participating — Dr. O'Rouorke Moderator

SUNDAY, JANUARY 18, 1970

9:30-12:00	Case Presentations

Contact: Arizona Heart Association, 1720 East McDowell Road,
Phoenix, Arizona 85006

The University of Southern California, Department of Psychiatry, Postgraduate Division, is offering a course in Phoenix. The course is entitled

MANAGEMENT OF EMOTIONAL PROBLEMS IN A MEDICAL PRACTICE

The course is designed to improve physicians' skills and provide them with many practical guidelines in detecting and managing emotional problems in patients.

TIME:	7:00 p.m. - 9:00 p.m.
DATE:	**Tuesdays** — January 13, 1970 through April 17, 1970.
INSTRUCTORS:	Howard Gray, M.D., Clinical Instructor in Psychiatry. Richard E. H. Duisberg, M.D., Associate Clinical Professor in Psychiatry, University of Southern California.
PLACE:	Arizona State Hospital.
TUITION:	$35.00 — the low tuition fee is made possible through a grant from the National Institute of Mental Health.

Registration should be submitted at least two weeks before the scheduled course is to begin, but late registration will be acceptable. The course is accredited by the American Acad. of General Practice.

If you have further questions, communicate directly with the Postgraduate Division or contact your local university representative, Howard Gray, M.D., Phoenix. Telephone: 252-2267.

Please mail your check for $35.00 to the Postgraduate Division of Psychiatry, 2025 Zonal Avenue, Collage B, Los Angeles, California 90033 — along with your name, address, phone number, type of practice, date of degree and medical school.

1970 ARIZONA CHEST DISEASE SYMPOSIUM

RAMADA INN
Tucson, Arizona
March 20, 21, 22, 1970

SYMPOSIUM PARTICIPANTS:

Professor C. H. Stuart-Harris
C.B.E., M.D., F.R.C.P.
The University of Sheffield
Sheffield, England

Henry N. Claman, M.D.
Associate Professor of
Medicine and Microbiology
University of Colorado
Denver, Colorado

Ernest K. Cotton, M.D.
Associate Professor of Pediatrics
University of Colorado
Denver, Colorado

C. M. Shy, M.D.
Chief of Epidemiology
National Air Pollution
Control Administration
Health, Education & Welfare

REGISTRATION — $15.00**

This includes two luncheons. Registration at this time enables us to have your badge and tickets prepared in advance, and eliminates waiting in the registration line.

**No registration fee will be charged for medical students, interns or residents; however, everyone who attends must register, whether or not a fee is required.

For further information and registration form, contact:

ARIZONA CHEST DISEASE SYMOPSIUM
P. O. Box 6067
Tucson, Arizona 85716

Institute of Gastroenterology, Good Samaritan Hospital
&
Section on Gastroenterology, Department of Medicine, St. Joseph's Hospital

GASTROENTEROLOGY DAY

Second Seminar

COLON DAY

January 23, 1970
Mountain Shadows

Moderator	Robert Sommerville, M.D. Section of Gastroenterology St. Joseph's Hospital, Phoenix, Arizona
8:30 A.M.	Newer Knowledge on the Utiology of Ulcerative Colitis Joseph B. Firsner, M.D. Professor of Medicine University of Chicago, Chicago, Illinois
8:50 A.M.	Ulcerative Colitis versus Granulomatous Colitis Joseph B. Kirsner, M.D.
9:10 A.M.	Ulcerative Colitis in Children Lawrence J. Shapiro, M.D. Good Samaritan Hospital, Phoenix, Arizona
9:30 A.M.	Medical Management of Ulcerative Colitis Joseph B. Kirsner, M.D.
10:10 A.M.	Surgical Management of Ulcerative Colitis Patrick T. Phalen, M.D.
10:30 A.M.	Intermission
10:45 A.M.	Question and Answer Period

THE AMERICAN CANCER SOCIETY, ARIZONA DIVISION, INC.

THIRTEENTH CANCER SEMINAR FOR DOCTORS

Thursday, January 22, 1970
University of Arizona College of Medicine
Tucson, Arizona

The faculty for the one day session will include:

Name & Position	Subject
Robert J. Huebner, M.D., Chief Viral Branch National Canver Institute of Health, Washington, D. C.	A Theory of Switched Off or Repressed RNA Tumor Virus Genomes as Causes of Cancer
Nathan A. Womack, M.D., Professor of Surgery, University of North Carolina, Chapel, Hill, N. C.	Progression in Cancer of the Breast
Arthur Haut, M.D., Associate Professor of Medicine, University of Arkansas College of Medicine, Little Rock, Ark.	Treatment of Chronic Hematologic Malignancies
William Trier, M.D., Associate Professor of Surgery, University of Arizona College of Medicine, Tucson, Arizona	Surgical Treatment of Prognosis Acute Leukemia

PANEL DISCUSSION will be as follows:

Oscar Thorup, M.D., Professor and Head, Department of Medicine, University of Arizona College of Medicine, Tucson, Arizona	Treatment of Prognosis of Acute Leukemia
Robert J. Huebner, M.D.	
Arthur Haut, M.D.	
William F. Denny, M.D., Association Professor of Medicine, University of Arizona College of Medicine	
Erle Peacock, M.D., Professor and Head, Department of Surgery, University of Arizona College of Medicine	The Surgery of GI Tract Malignancy
Charles Zukowski, M.D., Professor of Surgery, University of Arizona College of Medicine	
Charles Witte, M.D., Assistant Professor of Surgery, University of Arizona College of Medicine	
Nathan Womack, M.D.	

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The following 64 pages are reprinted from CALIFORNIA MEDICINE as an item in prospectus for a "Western Journal of Medicine," not yet in existence. It is proposed that articles of the kind shown here, with additional material from elsewhere in the western United States, be published in a supplement, to be called "The Western Journal of Medicine," which would be available at low cost for use in ARIZONA MEDICINE and in other selected journals from the Rocky Mountains westward, should they wish to use it. ARIZONA MEDICINE would of course maintain its present identity, treating "The Western Journal of Medicine" insert as additional material within its present cover.

Besides lowered cost, a great advantage of the combined circulation would be that the journal would attract writers who now place their scientific articles in publications that can offer wider readership.

New Concepts of Digitalis

CHARLES C. WYCOFF, M.D., *San Francisco*

■ *The data presented in this review have substantiated the following ideas:*

- *There is a direct relationship between digitalis dosage and myocardial contractile force. A small dose of digitalis produces a small increase of the contractile force of the heart and a large dose increases the force of the heart's contraction by a much greater amount, whether the heart is normal, has a poor reserve, or is in frank failure.*
- *Digitalis is of benefit to the patient with cardiovascular disease whether his heart is in failure or not.*

DIGITALIS HAS BEEN RESERVED in the past to slow the pulse of a patient with a rapid ventricular response during atrial fibrillation or flutter, and to aid the heart that is in frank failure. Frequently an attempt has been made to administer a "full digitalizing dose" since there has been a belief that a dose smaller than that is not effective. Over the past decade or two a body of data has been accumulating, in the laboratory and at the bedside, which has extended the use of digitalis. It has been demonstrated that digitalis, even in low dose, increases the ability of the heart to pump out the blood that comes to it. This effect of digitalis is produced in the normal heart, as well as the heart with pathologic changes but not in failure, and also in the heart which has failed. This paper is a review of the literature with the aim of supporting two ideas about digitalis. The first idea is that there is a direct relationship between digitalis dosage and contractile force of the heart; and the second is that digitalis is of benefit to the patient with heart disease but not in frank heart failure.

Relationship Between Digitalis Dose And Contractile Force of Heart

The idea that a "full digitalizing dose" of a cardiac glycoside must be given to achieve any effect on the myocardium has probably come from the observation that large doses of digitalis must be given to slow the ventricular response of the heart

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Submitted, revised, 4 September 1969.

Reprint requests to: 900 Hyde Street, San Francisco, Ca. 94109.

during atrial fibrillation and flutter. However, that which holds true for the conduction effect of digitalis does not necessarily apply to the inotropic effect of the drug. Starr[1] summarized his views on the dose of digitalis after reviewing his studies with the ballistocardiograph in patients: "The idea of the digitalizing dose, the conception that a certain amount of digitalis, calculated from the patient's weight, had to be given before there was *any* digitalis action has proved wrong. This idea was based on observations made on heart rate. Measuring the forces, one finds that much smaller doses than this have definite effects on the heart's performance in many patients, often in the absence of changes of rate."

An instrument has been developed, the strain gauge, which can be sutured onto the ventricle of the heart to measure the force of the muscular contraction. This device makes it possible to assess the increase of the force of ventricular contraction produced by digitalis. In 1950, Walton et al[2] sutured a strain gauge to the right ventricle of normal dogs and found a direct relationship between the dose of all cardioactive drugs tested and an increase of contractile force of the heart. They found with ouabain that 0.25 of a cat unit increased the contractile force 25 percent above normal, 0.75 of a cat unit raised the contractile force 65 percent above normal and 1.25 cat units raised the contractile force 100 percent above normal. They stated: "The electrocardiograms did not show distinctive changes before development of substantial increases in contractile force. In a few instances, maximal contractile force changes preceded by a distinct interval any significant manifestation of the typical ECG changes."

Williams et al,[3] in 1966, studied the contractile force of the right ventricle in normal dogs and found that 60 percent of the toxic dose of ouabain raised the contractile force 43 percent above the control level, 80 percent of the toxic dose raised the contractile force 48 percent above normal, the toxic dose raised the ventricular contractile force 65 percent above normal, and when the arrhythmia was controlled with intravenous potassium, and more ouabain was given, the contractile force rose to 84 percent above normal.

An increase of contractile force of the ventricle causes the heart to empty more rapidly. The decrease of emptying time can be used as a measure of the effect of a given dose of digitalis on the contractile force of the heart. Weissler et al,[4] in 1965, studied 30 normal college males and measured the total duration of left ventricular systole from the onset of ventricular depolarization to the closure of the aortic valves by simultaneously recording the electrocardiogram and the phonocardiogram. Eight hours after an intravenous dose of deslanoside, they found that the emptying time had been shortened 14 milliseconds by the action of 0.4 mg of the drug, 20 milliseconds by 0.8 mg and 34 milliseconds by a 1.6 mg. They summarized their findings: "The mean response in the duration of each of the phases of systole during the first eight hours following administration of deslanoside proved to be dose-dependent."

Less than a "digitalizing dose" of lanatoside-C (Cedilanid®), 0.8 mg, has been shown to be effective in improving the cardiac status of patients with damaged hearts. Lagerlof and Werko,[5] in 1949, administered such a dose to five patients who were in failure. They measured the cardiac output before and after digitalization and found: "The cardiac output invariably rose in the cases in heart failure while the response in the other cases sometimes was in the direction of increase, sometimes in the direction of decrease."

Malmcrona et al,[6] in 1966, gave 0.8 mg of lanatoside-C (Cedilanid®) to ten patients who had acute myocardial infarction and a substantial fall in arterial pressure but without left ventricular failure or cardiogenic shock. They found a rise in blood pressure after the administration of the digitalis and summarized their findings: "This study indicates that a moderate digitalis dose, given intravenously to patients with myocardial infarction, may be beneficial rather than dangerous, even in the absence of overt failure, as judged from the hemodynamic effects."

It can be deduced from these studies that one of the physiological effects resulting from the administration of digitalis, an increase in contractile force of the ventricle, is dose-dependent: a small dose of the drug produces a small increase of the contractile force and a large dose results in a large increase in the contractile force of the ventricle.

Beneficial Effect of Digitalis To the Heart Not in Failure

General Considerations

Digitalis has been shown to increase the cardiac output of the heart in failure and also has been shown to decrease the cardiac output of the heart which is not in failure.[7,8] It was therefore assumed that digitalis was beneficial to the heart in failure and detrimental to the heart not in failure. This was an erroneous assumption regarding the heart not in failure since the fall in cardiac output is probably due to a peripheral vascular constriction that digitalis produces.[8,9] Such vascular constriction can result in a diminished venous return to the heart and also an increased resistance to the arterial outflow.

There has been considerable experimental work in animals and observation in humans demonstrating that digitalis increases the contractile force of the heart whether it is normal, abnormal but not in failure, or in frank failure. This increase in contractile force has been demonstrated to be beneficial to the chronically stressed heart, as well as to the heart with poor reserve.

Cotten and Stopp,[10] in 1958, demonstrated that digitalis increases the ability of the normal heart to pump out the blood that comes to it. They studied the effect of digitalis in normal dogs by measuring the myocardial contractile force and also by progressively increasing the left atrial pressure and measuring the stroke work as the heart load increased. They summarized their findings: "The increase in left ventricular contractile force provoked by ouabain and the higher ventricular function curves obtained after injection of this glycoside show conclusively that ouabain stimulates the non-failing heart of the dog with a complete circulatory system."

Stewart et al,[11] in 1938, studied 13 patients with compensated heart disease by digitalizing them over 24 hours and recording their cardiac output, electrocardiograms and heart size. They concluded that the factor common to all patients as a result of digitalis was an increase of work per beat.

Sokolow et al,[12] in 1942, studied four patients who had been in failure and were being maintained with digitalis. Discontinuing digitalis allowed them to go into failure again. To evaluate failure, these investigators used the vital capacity measurement, venous pressure, hepato-jugular reflux, circulation time, weight and clinical evaluation. They stated: "Continuous digitalization is of value in preventing recurrences of cardiac failure in ambulatory patients with sinus rhythm. It is unwise to omit this drug in patients with diminished cardiac reserve who have previously shown failure, even though the patient is free of symptoms."

Erickson and Fahr,[13] in 1945, studied 39 patients who had no evidence of failure but had enlarged hearts and a slowed circulation time. They found that digitalization improved the mechanical efficiency of the hearts of 87 percent of the patients studied. "We believe," they said, "that digitalis is definitely indicated for organically diseased and enlarged hearts which appear compensated, when the circulation time, as measured by the calcium gluconate arm-to-mouth method, is greater than 16 seconds."

Hedlund,[14] in 1952, studied 12 patients with latent cardiac insufficiency (no overt failure) using an exercise test with determination of oxygen consumption and oxygen debt. He found that digitalization effectively decreased the oxygen consumption during work and also decreased the relative oxygen debt. He summarized, in an abstract to the author: "Therefore, it is expedient not to suspend glycoside therapy, even when the patient is in good clinical condition and is compensated. As in the case of cardiac decompensation, the patient should receive an uninterrupted treatment with the cardiac glycosides."

Braunwald et al,[15] in 1961, studied 21 patients with heart disease, who were not in failure, by suturing strain gauges to their right ventricles. They found that acetyl strophanthidin increased the contractile force an average of 87 percent above control and Cedilanid® increased the contractile force 31 percent. They summarized their views: "In view of the positive inotropic effect of digitalis on the non-failing heart, the fear of cardiac depression when these drugs are used 'prophylactically' . . . would not seem to be warranted. Thus, the exhibition of cardiac glycosides does not appear to be contraindicated in patients without overt heart failure in whom the development of heart failure is feared because of the superimposition of an excessive hemodynamic burden resulting from an acute infection or surgical procedure. Indeed, the demonstration in the present study of the substantial augmentation of contractile force provided by digitalis has led to the establishment of a policy at the National Heart Institute to digitalize all patients prior to intracardiac surgery."

Selzer and Malmborg,[16] in 1962, studied 15 patients who had been in left heart failure and were relieved of their frank failure by bed rest, diuretics and low salt. They recorded the patients' cardiac pressures and performance under exercise. They observed the results before digitalization: "In all patients, the abnormal circulatory dynamics were accentuated by exercise, as evidenced by the further rise in left atrial and pulmonary arterial pressure, and an inadequate increase in cardiac output." Also they summarized the results after digitalization: "Ten patients showed significant improvement consisting of lowering left atrial and pulmonary arterial pressures and an average increase in resting cardiac output of 40 percent. Five patients showed no significant hemodynamic change."

Kahler et al,[17] in 1963, studied the oxygen debt that three compensated cardiac patients developed from exercise during the time that they were not receiving digitalis, when they were receiving digitalis, and when they were receiving placebos, in various sequence. "All had inactive rheumatic valvular disease, cardiomegaly, and a history of cardiac decompensation some months or years previously, but had none of the clinical signs of congestive heart failure at the time of the study. These three patients were selected because they were capable of performing light physical activities without cardiac symptoms in the absence of digitalis therapy." The authors summarized their findings and opinions: "In all patients the oxygen debt was smaller during the period of digoxin administration, although the external work performed was identical. . . . The accumulation of a smaller oxygen debt following exercise while these subjects were receiving digoxin indicates that the functional status of their circulatory system was improved by the drug. . . . It would appear that digitalis administration is beneficial to at least some patients who have cardiac disease and enlarged hearts and some decrease in cardiac reserve without signs or symptoms of heart failure."

Mason and Braunwald,[18] in 1963, studied ten patients when they were not digitalized and when they were digitalized. They found that digitalis increased the myocardial contractile force in those unanesthetized humans with a normal heart and those with an abnormal heart that was not in failure. They studied the rate of change of the intraventricular pressure which is an index of the contractile force of the heart. They summarized their findings: "In four patients without heart disease and in two patients with minimal cardiac abnormalities and normal right ventricular function, 0.30 to 0.60 mg ouabain elevated the right ventricular peak rate of change (dp/dt) by 9.9 to 73.5 percent (average = 31.5 percent of control values). In four patients with uncomplicated atrial septal defects, in whom the left ventricular hemodynamic burden and left ventricular function were normal, 0.60 mg oubain elevated the left ventricular peak dp/dt by 26.3 to 48.8 percent (average = 35.5 percent) of control value. These observations in intact, unanesthetized subjects indicate that ouabain is capable of stimulating the contractility of the non-failing and of the normal human heart."

Murphy et al, [19] in 1964, studied nine patients with cardiac disease by catheterizing the right and left (transseptal) sides of the heart. Three of the patients were in heart failure and six were compensated. Various indices were studied before and after digitalization—cardiac index, stroke index and stroke work, stroke power, mean systolic ejection rate, left ventricular end-diastolic pressure, first derivative of left ventricular systolic pressure (dp/dt), mean systolic ejection period, systemic arterial pressure and ventricular function points. They commented on their findings: "It is of clinical interest that evidence of augmented ventricular performance was found in our patients with cardiomegaly but no detectable clinical heart failure. Improvement of ventricular performance in these cases after digitalization was characterized mainly by an increase in the rate of rise of left ventricular pressure and a general tendency of ventricular function points to shift left and upward on the stroke work-left ventricular diastolic pressure diagram."

Sonnenblick et al,[20] in 1966, studied six patients who had previously had operations on the heart but were in a compensated state. Metal clips had been sutured to the ventricular surface so that cineradiographs could be taken to record the velocity of contraction and this rate was related to the force of contraction as determined by the arterial pressure. The studies were done before and after digitalization. They summarized their findings: "It was observed that ouabain always augmented myocardial contractility as reflected in the force-velocity relation. Velocity of shortening increased an average of 77 ±5 (SEM) percent. . . . It is concluded that the fundamental action of digitalis glycosides is to augment the contractile state of the heart, whether normal or failing, but that in the absence of heart failure this improvement is not translated into an increase in cardiac output."

Reindell and Konig,[21] in 1967, reported on studies of several hundred volunteers and patients during which they determined the myocardial reserve by doing exercise tests. During the exercise tests, they measured the heart rate, the heart size and the oxygen uptake. They found that patients who were not in failure but who had fixed hypertension, coronary insufficiency or branch blocks, or who had had myocardial infarction, showed performance tests that were well below the normal for their ages. In other words, a "loading insufficiency" developed. These patients were shifted to the normal or near normal status by digitalization. These investigators summarized their studies: "According to these findings there is no doubt that the uneconomical mode of operation of the heart which becomes insufficient of loading is decisively improved due to application of digitalis. This results in the basic demand that the heart which is insufficient on loading should be digitalized in the same way as the heart which is insufficient at rest."

Mason,[22] in 1968, summarized the mode of action of digitalis: "Since digitalis has the same fundamental action on both normal and failing hearts, the view that the drug has a harmful effect on the non-failing heart cannot be given credibility. Digitalis lowers the oxygen debt following exercise in patients with cardiomegaly but without heart failure, indicating that the functional status of the circulatory system may be improved by the drug in at least some patients without overt failure. In addition, digitalis may be of potential clinical value in preventing the development of ventricular hypertrophy in patients with aortic valvular disease or hypertension without heart failure, since the drug reduces the degree of mortality from heart failure and the degree of ventricular hypertrophy resulting from a chronic pressure load in experimental animals, further, the belief that the administration of digitalis in special situations may be helpful in certain cardiac patients without failure is gaining in prevalence. Thus, prophylactic digitalization may protect the myocardium in these patients in the face of the depressing effects of anesthesia and operation, serious illnesses such as pneumonia, and the hypervolemic state during pregnancy."

The benefit of digitalis to the acutely stressed heart of the dog was shown by Selzer et al,[23] in 1953. During thoracotomy, they measured the amount of constriction that could be applied to the pulmonary artery and the length of time the constriction could be tolerated before failure occurred. The studies were done before and after ouabain was administered. They stated: "It seems reasonable to conclude from the results of this study that the group of digitalis drugs may exert a favorable effect upon the normal heart during unusual stress. It seems difficult to visualize a clinical situation where such a property of digitalis would appear useful. However, if a similar action could be demonstrated upon the competent hypertrophied heart, where such an effect could conceivably be much more useful, then earlier prophylactic use of digitalis could be justified in compensated heart disease."

In 1908 and 1929, Cloetta[24,25] found that digitalis prevented the chronically stressed rabbit heart from enlarging as much as the undigitalized stressed heart. He avulsed a single aortic valve in the animals and maintained half of the group on digitalis. At the end of one year, the untreated animals had an increase of heart size 80 percent above the normal unstressed rabbit heart and the digitalis-treated animals had only a 38 percent increase of heart size above normal. In addition, acute performance tests of the hearts were made and the results were summarized: ". . . one finds that the crippled digitalis treated heart is almost equal to the normal; while the defective heart without digitalis treatment is much more rapidly exhausted. The capacity of the former is nearly double that of the latter, a fact of great importance in practice. This should be sufficient to induce prophylactic treatment with digitalis in all early cases of endocarditis which are apt to terminate in valvular lesions."

Williams and Braunwald,[26] in 1965, studied chronic heart strain in rats by constricting the abdominal aorta, which resulted in hypertension. Some of the rats were maintained on digitalis. Their results were similar to those of Cloetta. Fewer of the digitalized rats died from heart failure and the weight gain of the digitalized hearts was less than the undigitalized hearts.

Preoperative Digitalis Benefits The Patient with Myocardial Disease

The stress of surgical operation on the myocardium is considerable with frequent occurrence of hypoxia,[27] hemorrhage, and depression from anesthetic drugs.[28] These strains are detrimental to the patient with myocardial disease, as revealed by a high incidence of postoperative cardiac complications. Sufficient data have now been accumulated to show that preoperative digitalization protects the hearts of those patients who have cardiac disease but are not in failure.

The thoracotomy patient

Wheat and Burford,[29] in 1961, reported on a retrospective study of 439 patients who had thoracotomy. These investigators summarized their findings: "Cardiac complications following major intrathoracic resections can be reduced from 20 to 10 percent over the age of 55 by prophylactic preoperative digitalization. . . . All patients over 60 years of age in whom a major intrathoracic resection is contemplated should be digitalized routinely preoperatively."

Heilbrunn and Hardin,[30] in 1963, retrospectively reviewed 89 patients over 70 years of age who had thoracotomy. They found that non-digitalized patients had a 24 percent incidence of postoperative arrhythmia and the arrhythmia caused or contributed to the death of 4 percent of the total number of undigitalized patients. The patients who had been digitalized preoperatively had a postoperative incidence of arrhythmia of 1 percent which did not contribute to or cause fatality. Heilbrunn and Hardin summarized their results: "We believe that prophylactic digitalization is indicated in patients over 70 who undergo thoracic procedures and is of value in avoiding and controlling postoperative arrhythmias."

Bergh et al,[31] in 1967, retrospectively reviewed 229 cases of pneumonectomy, in 148 of which the patients had had prophylactic digitalization. The incidence of postoperative atrial fibrillation was 10 percent in the digitalized group and 20 percent in the non-digitalized. The patients were digitalized on the day of operation after surgery had been completed.

Burman,[32] in 1965, reported on 244 patients over the age of 40 who had major thoracic surgical procedures without extracorporal circulation. One hundred and fifty-nine of them were digitalized to the limit of tolerance and 85 were either incompletely digitalized or not digitalized at all. The incidence of arrhythmias or congestive failure that occurred during the first three weeks postoperatively in the fully digitalized group was 3.2 percent and in the other group was 16.4 percent. The mortality from cardiac complication in the fully digitalized group was 1.3 percent and in the other group was 7 percent. Burman also reported on the results with cardiac operation with and without extracorporal circulation. He stated: ". . . It is far safer to digitalize a patient unhurriedly four or five days before surgery . . . than to do so haphazardly in the face of impending disaster." In summary he stated: "Each group was divided into two categories, those who received preoperative digitalization and those who did not. The subsequent course of each group was compared and found to be strikingly dissimilar in favor of those receiving preoperative digitalis."

The general surgery patient

Brockner and Christiansen,[33] in 1965, reported on 235 patients who had surgical operation for malignant disease of the stomach. In some of the patients arrhythmias and heart failure which required digitalization developed in the postoperative period. Of the group with no pre-existing cardiac disease, 4 percent required digitalization after the operation. Of the group with cardiac disease but not in heart failure preoperatively, 50 percent required digitalization after the operation. The authors stated: "The conclusion is drawn that digitalis should be administered before major operations if one or more of the following abnormalities is present: (1) a history of cardiac symptoms; (2) electrocardiographic changes suggestive of myocardial degeneration; (3) enlargement of the heart demonstrated by roentgen examination of the thorax."

McCord,[34] in 1967, did a retrospective study of 186 patients over 60 years of age who had partial colectomy. Sixty-eight of them were found to have coexistent cardiovascular disease. Thirty-nine of the patients with coexistent cardiovascular disease were not digitalized. The morbidity rate for this group was 46 percent and the mortality rate was 18 percent. Twenty-nine patients were digitalized preoperatively. The morbidity in this group was 17 percent and the mortality was 7 percent. McCord summarized his results: "The findings in this study suggest that each elderly patient who is to have a major surgical procedure should be evaluated for the presence of cardiovascular disease. If evidence of such disease is found, the morbidity and mortality from postoperative cardiovascular complications can be reduced by the use of prophylactic digitalization."

Effect of Digitalis in Shock

Data have been accumulating that reveal digitalis is of benefit in hypotension resulting from trauma, hemorrhage, infection, anoxia, and anesthesia.

Keyl and North,[35] in 1957, found that pretreatment of rats with digitalis was effective in lowering the mortality rate from traumatic shock produced by tumbling.

Crowell and Smith,[36] in 1964, bled 100 dogs to shock levels and measured the oxygen deficit developed by the shock as an assessment of the degree of shock. The blood that had been withdrawn was reinfused after the pre-determined oxygen deficit was produced and half of the animals were then digitalized. At an oxygen deficit of 140 ml per kg, all the digitalized animals survived and all the undigitalized died.

Baxter et al,[37] in 1966, demonstrated a myocardial depressant factor in the blood of dogs that had received a 50 percent skin burn 24 hours before cross circulation with normal dogs. The blood of the burned animals produced a 53 percent fall of cardiac output in the normal animals within five minutes after the start of perfusion. These animals were not treated to assess the effect of digitalis on the fall of cardiac output. However, Brand and Lefer,[38] in 1967, found a myocardial depressant factor produced in the blood of cats by hemorrhagic shock. They were able to completely counteract this factor with digitalis. They used the cat papillary muscle as the test device.

Levin and Painter,[39] in 1966, reporting on 28 soldiers (ages 17 to 24 years) treated for meningococcal disease, noted that ten had hypotension which responded in most instances to digitalis. They summarized: "Previous emphasis on peripheral vascular collapse in the etiology of shock in this disease has been at least partially misplaced. A primary decrease in cardiac output appeared to be a major factor in the hypotension seen in the majority of cases in this series. Recommended management of hypotension includes placement of a central venous catheter with continuous monitoring of central venous pressure, intravenous administration of a rapidly acting digitalis preparation in full digitalizing dosage with electrocardiographic monitoring, and use of a continuous isoproterenol infusion to maintain cardiac output in those patients not showing adequate response to digitalis alone."

Hernandez et al,[40] in 1968, used excised atrial muscle of non-failing human hearts as test systems. In 11 cases the heart had not been digitalized and in 15 it had been digitalized before the atrial strips were excised. The muscle strips were preoxygenated for one hour, rendered hypoxic for one hour, and then aerated for one hour. Measurement of the contraction response was recorded throughout. Following anoxia, the undigitalized strips recovered 30 percent of the equilibration contraction level, but the predigitalized strips recovered 62 percent of the equilibration level.

Goldberg et al,[41] in 1962, found that halothane caused a progressive arterial hypotension and decrease of the contractile force of the dog heart with deepening anesthesia. A concentration of 0.2 percent halothane depressed the contractile force by 33 percent, 1 percent halothane depressed the contractile force 73 percent, and 2 percent halothane depressed the contractile force 80 percent. They did the same studies after digitalization and summarized: "Pretreatment with digoxin significantly diminished the negative inotropic and hypotensive effects of 1 and 2 percent halothane anesthesia."

Digitalis Protects in Coronary Occlusion

Cronin and Zoster,[42] in 1965, produced cardiogenic shock in 23 dogs by coronary embolization and then digitalized some of the animals. They summarized their results: "Rapid digitalization . . . caused a substantial elevation in arterial blood pressure and cardiac output in every animal. . . . This restoration of the shocked animals' hemodynamic status toward normal was associated with a marked increase in left ventricular work in all dogs and an average lowering of the end-diastolic left ventricular pressure. . . ."

Marano et al,[43] in 1966, used a comparable technique of coronary embolization in 28 dogs to produce cardiogenic shock. Ouabain produced a significant rise of cardiac output, central aortic pressure and dp/dt in ten of eleven animals. They summarized their findings: "It is concluded that rapid digitalization may be of definite, though transitory, benefit in improving cardiac output and aortic pressure in acute myocardial infarction with shock, even in the absence of hemodynamic evidence of congestive heart failure."

Aldinger,[44] in 1967, prophylactically digitalized 24 dogs and then occluded the artery to the left ventricle. Ventricular fibrillation occurred in 63 percent of the non-digitalized dogs but fibrillation occurred in only 25 percent of the predigitalized dogs. In addition, he stated: "The digitalized animals developed and maintained more myocardial tension than the untreated group when subjected to the stress of acute coronary occlusion."

Malmborg,[45] in 1965, reported on a study of 38 men, aged 40 to 58, who had symptoms of coronary insufficiency but were not in apparent heart failure. He stated: "The results indicate that even at rest acute digitalization had a small but significant effect on both the flow and the intracardiac pressures. During exercise the effect was more marked as evidenced by a highly significant lowering of the heart rate." His data show that some patients were in occult failure at rest and others went into failure with exercise, and digitalis aided both these groups. He summarized: "A beneficial effect of digitalis upon the hemodynamics could be demonstrated in 57 percent and on the subjective symptoms in 53 percent of the studied cases. . . . The present results prove that digitalis therapy was actually of value in the therapy of a certain number of patients with coronary heart disease even when clinical signs of congestive failure were lacking."

Discussion

These data show that small doses of digitalis increase the contractile force of the heart and larger doses produce an even greater increase in the contractile force. Also these data show that digitalis is beneficial to patients who have heart disease but are not in frank heart failure.

A very important clinical application of these ideas is the prophylactic digitalization of patients with cardiac disease who are not in heart failure and are to have an operation. These data show that such patients who are digitalized have a lower incidence of morbidity and mortality than the patients with cardiac disease who are not digitalized preoperatively.

Heilbrunn and Hardin[30] expressed belief that all patients over the age of 70 should be digitalized preoperatively if they are to have thoracotomy. Their patients over 70 years of age who had preoperative digitalization had a decidedly lower incidence of cardiac arrhythmia and mortality therefrom than did those who were not digitalized preoperatively. Burman[32] also found a pronounced lowering of cardiac complications and mortality therefrom in patients with thoracotomy who were completely digitalized before operation. In addition, he pointed out the desirability of slowly digitalizing the patients preoperatively rather than hurriedly doing so when the cardiac complications occurred. Brockner and Christiansen[33] found that patients who were not in heart failure and were operated on for malignant disease of the stomach were 12 times as likely to need postoperative digitalization if they had a history of cardiac symptoms, or had electrocardiographic changes suggestive of myocardial degeneration, or enlargement of the heart as seen roentgenographically. In addition, these observers recommended preoperative digitalization if one or more of these findings were present even though the patient had no sign of heart failure. McCord[34] found that patients over 60 years of age who had cardiovascular disease and underwent partial colectomy had morbidity and mortality rates halved by preoperative digitalization. He considered the patients to have cardiovascular disease if there were positive findings in two of four items of examination: history, physical examination, roentgenogram and electrocardiogram. An isolated finding of electrocardiographic evidence of an old myocardial infarction also established a diagnosis of cardiovascular disease.

The stresses that the patients are subjected to during operation are many. Some that are particularly detrimental to the cardiovascular system are the diminution of tissue perfusion resulting from blood loss, the hypoxia that results from diminished respiration, and the depression of the myocardium resulting from the action of the anesthetic drugs. These stresses are partly responsible for the high incidence of morbidity and mortality that occurs during and after operation in patients who have preexisting cardiovascular disease. Even with the best of management these stresses occur all too frequently. It is possible to lower the incidence of morbidity and mortality following operation by preoperative digitalization of patients who have evidence of cardiovascular disease.

Another clinical application of some of the above summarized data is in the patient with chronic hypertension. In such a patient a constant increase in work load is put on the heart, which may eventually result in myocardial hypertrophy. Digitalis, by increasing the contractile force of the heart, can reduce hypertrophy and failure when chronic stress is put on the heart, as was demonstrated by Cloetta[25] and Williams and Braunwald.[26] These investigators stressed the hearts of animals by avulsing one aortic valve leaf in one series and constricting the abdominal aorta in the other series. Digitalis limited the resultant myocardial hypertrophy and reduced the mortality from heart failure. The same physiological principles should apply to the stress of chronic hypertension in humans. Therefore, hypertensive patients should have longer lives and less disability when maintained on digitalis.

Reindell and Konig[21] showed that the function of the heart is diminished in patients who have had myocardial infarction and apparently have recovered. These investigators also found that digitalis was effective in returning the function of hearts damaged by myocardial infarcts back to a near normal level. Another observer, Malmborg,[45] found that digitalis had a beneficial effect on the hemodynamics and subjective symptoms of patients with coronary insufficiency. Apparently the increase of contractile force produced by digitalis causes a better perfusion of the ischemic heart as well as the heart damaged by a myocardial infarct.[42-45] Digitalis is of benefit when given to the patient who has angina, an acute myocardial infarction[46] or a healed myocardial infarct, even when the heart is not in failure.

Toxicity is the major deterrent to the use of digitalis. It is known that arrhythmias produced by digitalis can be lethal to the patient with heart failure, particularly when a low level of potassium is present in the blood.[47] Also, it has been shown in animal studies that a dose of digitalis that produces an arrhythmia can decrease the flow of blood in the coronary artery.[48] Therefore, the dose of digitalis should be kept below the arrhythmic dose. It is imperative that the dose of digitalis be individualized for each patient. The "digitalizing dose" has been assessed as 60 percent of the toxic dose.[49,50] However, it is now recognized that even small doses of digitalis have a positive inotropic effect on the heart and produce an increase in the contractile force. Therefore, it is possible to get a beneficial effect from digitalis in a dose much lower than that which was considered a digitalizing dose in the past. When the maximum effect of digitalis is desired, the dose can be raised slowly, preferably over days, until toxicity occurs and then a slightly lower dose can be administered. Nausea, vomiting, yellow vision or scotomata will occur frequently as a symptom of toxicity before arrhythmias occur. However, the pulse must be checked for ectopic beats, bigeminy and runs of tachycardia, and the electrocardiogram can be watched for prolongation of the PR interval or for frank A-V dissociation. Many patients do not have gastrointestinal or nervous system changes before arrhythmias.

A "full digitalizing dose" may become a toxic dose if a patient goes into failure. Olson et al,[51] in 1955, reported a study which showed that in dogs with heart failure ventricular tachycardia developed with one-third the dose of cardioactive drug that was needed to produce the same degree of toxicity in normal dogs. These investigators did not report the blood level of potassium in the animals studied.

Other situations besides decompensation that make the heart more sensitive to digitalis are low level of serum potassium, high level of calcium, hypoxia, oliguria, acute myocardial infarction, and individual variation.[52-59]

The idea that a "full digitalizing dose" must be given to produce a beneficial effect on the heart presupposes that the only effect of digitalis is the slowing of the rate of the heart in failure and arrhythmias. It is now known that the increase in contractile force is the primary beneficial effect of digitalis and the slowing of response of the ventricle in atrial fibrillation and flutter is one of the lesser effects. Even small doses of digitalis produce an increase of contractile force, whereas much larger doses are required to achieve a ventricular slowing in atrial fibrillation.[60] The administration of doses of digitalis smaller than those required to slow the ventricle in atrial fibrillation are effective in improving the function of the heart. The smaller doses of digitalis should not be considered as homeopathic doses.

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Learning Disorders as a School Health Problem

Neurological and Psychiatric Aspects

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■ *Broadened concepts of intellectual functions have shown that many varieties of mental subnormality may be preventable or subject to improvement with proper treatment. Many types of neurologic dysfunction are accompanied by learning disorders based on specific intellectual deficits.*

A more refined delineation of the higher cerebral functions of each child with a learning disorder provides the basis for improved specific remedial educational techniques. Such detailed assessment of higher functions of the nervous system can be greatly enhanced by the appropriate special evaluations carried out by well trained psychologists, speech pathologists and educational consultants, working in cooperation with physicians.

The varieties of adjustment problems of children and emotional impact of a learning disorder should be recognized as early as possible and treated appropriately. Motor and perceptual-motor therapies may have limited value in some cases but may be harmful if indiscriminately applied. Psychotropic drugs have a relatively limited place in the management of learning disorders but may be immensely valuable in some cases by helping to control specific behavior problems which interfere with learning processes.

Physicians have a major responsibility to provide help and leadership in dealing with learning disorders.

MOST ESTIMATES PLACE the incidence of mental retardation, as customarily defined on the basis of an intelligence quotient score below 70 on a standard test, at approximately 3 percent of the total population.[88, 114] However, Zigler has pointed out that the actual incidence of mild grades of mental retardation appears to be much greater than would be predicted on the basis of a theoretical distribution pattern for "intelligence" in our society.[143] Many borderline forms of mental subnormality are often more obscure and undiagnosed. These milder learning difficulties afflict a much larger group of children, probably eight to ten times greater than the number with more obvious, more profound degrees of mental retardation.[52,77]

In a broad sense, the concept of mild mental retardation may be properly extended beyond the usual simple I.Q. classification (50 to 70) to include children with specific, often severely handicapping learning disabilities, such as "developmental dyslexia," despite an I.Q. score lying within the "normal" range or higher. This broader concept incorporates the definition of intelligence on a multilateral pattern of learning and memory and performance functions which may be pliable and subject to modification in various ways. It contradicts the older notion of intelligence as a more or less unitary level of capacities which remain static, rigidly fixed for each individual, from early infancy. It contradicts and condemns the traditional sterile doctrine of viewing mental retardation as "an unmodifiable cerebral condition which led to incurable behavioral inadequacy"—that is, a global intellectual subnormality. [15]

The importance of this subject lies not only in its present and apparently increasing prevalence, but also in the generally higher individual potential which may be realized through the earliest possible detection, adequate evaluation, and appropriate remediation. It has been amply demonstrated that mild mental subnormality, when neglected or mishandled, plays a heavy contributory role in psychiatric illness, addiction, delinquency, crime, and other economic waste.[87,103,104]

Children with milder learning disorders often present difficult problems to physicians, both in public health settings and in private practice. All physicians should work vigorously toward a more sophisticated understanding of these problems.[52,61,108]

Etiology

That learning problems may result from many causes has been increasingly apparent. Traditional views of the classification of mental retardation as *either* exogenous *or* endogenous have been largely replaced by a broader understanding of the many factors which influence learning processes.[61,81]

These potential etiologic factors include ethnic and cultural influences, socio-economic status, educational facilities, family relationships, individual temperament and behavior patterns, and emotional and motivational factors, as well as a large variety of more subtle disorders of the central nervous system.[52]

Cultural-Familial Retardation

By far the largest group, the "cultural-familial" form of mild mental subnormality is practically confined to socio-economically and educationally disadvantaged families. The long-standing question in these cases about the relative etiologic importance of hereditary and environmental factors remains largely unsettled, along with the question about whether these individuals really differ essentially from the normal population in the qualitative aspects of their cognitive functions.[103]

Quite often, gross deficiencies in parental care and training of children are encountered in disadvantaged families.[79] As enumerated in a recent report by the Group for the Advancement of Psychiatry,[61] specific sociocultural factors related to the family setting include the following:

- Insufficient or discontinuous mothering with physical neglect.
- Distorted patterns of child rearing with psychotic or retarded parents.
- Family disorganization: absent members; antisocial behavior in one or more family members.
- Social isolation of family and family members.
- Poverty, crowding, noise, lack of privacy, preventing personal ownership and control of physical *objects* (toys, games, books, clothes, beds), as well as control of *space* and *time.*

Many slum children come to school with dialectic differences and also with behavior patterns which have been essential to their growth and sur-

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Presented as part of a Symposium on Learning Disorders before a combined meeting with Section on General Practice co-sponsored by the American Academy of Pediatrics, Chapter 11, and the Southwestern Pediatric Society at the 98th Annual Session of the California Medical Association, Los Angeles, March 15 to 19, 1969.

Reprint requests to: 909 Hyde Street, San Francisco, Ca. 94109.

vival within their home or neighborhood environment. Their heightened distractibility and limited techniques for impulse control may seriously interfere with ordinary classroom learning. Other subtle perceptual and conceptual deficits frequently complicate the learning problems of these children.[23]

Brain Damage

Aside from possible hereditary neurological weaknesses, socioculturally disadvantaged children generally have a high risk of organic factors as a result of nutritional inadequacies, gestational insults, postnatal infection, cerebral trauma, and frequently substandard medical care. Similar subtle and generally unrecognized structural damage of the brain also occurs during the fetal and perinatal life of children in middle and upper economic class families.[88,94]

In a retrospective study Kawi and Pasamanick showed that complications of pregnancy, premature birth, and abnormalities of the prenatal and paranatal periods were far more frequent among cases of reading disability than among controls. Particularly important factors were found to be the toxemias of pregnancy (pre-eclampsia, hypertensive disease), bleeding before the third trimester, placenta praevia, and premature separation of the placenta. Kawi and Pasamanick concluded that "there is a continuum of reproductive casualty with a lethal component consisting of abortions, stillbirths, and neonatal deaths, and a sublethal component consisting of cerebral palsy, epilepsy, mental deficiency, and behavior disorders in children."[69,70]

Recently Towbin reported correlations of clinical case material with over 600 fetal (stillborn) and neonatal brain specimens studied, using a technique of whole-brain serial histologic section, which made possible the consistent identification and the geographical localizations of focal lesions, large and small.[132] He showed that two types of damage commonly occur: (1) in the premature fetus and newborn (25 to 35 weeks gestation), the usual hemorrhagic infarction chiefly involves the periventricular white matter and basal ganglia, due to the vulnerability to hypoxia of the highly vascular deep, rapidly developing deposits of germinal matrix tissue; (2) in infants born at full term the cerebral cortex is relatively more vulnerable to hypoxic damage because of the shift of biologic activity and vascularity during this stage of maturation.

Towbin's study provides evidence that neonatal cerebral damage often has its origin prior to labor. These pathological findings indicate that the frequent and paradoxical occurrence of cerebral palsy and organic mental retardation in infants having a history of uncomplicated non-cyanotic delivery may be due to prenatal cerebral hypoxic damage.

Towbin pointed out that lesser degrees of hypoxic injury may escape detection even microscopically, that the depletion in the nerve cell population may be subtle and unrecognizable. An overall loss of neurons up to 10 percent cannot be easily adjudged, even though the loss may amount to millions of nerve cells. The most differentiated, most highly specialized neurons are the most vulnerable ones of the entire body to hypoxic injury.[132]

While lethal prenatal cerebral lesions contribute heavily to the high incidence of neonatal mortality, lesser grades of hypoxic prenatal cerebral damage may be largely asymptomatic during infancy. Delays in language and motor development may be the first clear indications of subtle cerebral dysfunction and future learning problems based on prenatal cerebral damage.[139]

Genetic Abnormalities

In recent years a number of chromosomal abnormalities have been identified in some relatively uncommon syndromes which are accompanied by mental subnormality,[22,25] also several inborn errors of metabolism which critically affect cerebral function have been described and delineated.[111] These studies have shown clear indications that some varieties of severe mental retardation may be preventable with early diagnosis.[52,111] Many issues have been raised by these studies, and many questions about the role of hereditary factors in learning disorders still remain unanswered.[7,44]

Specific Learning Disorders

"Specific developmental dyslexia" probably has been the most intensely studied, as well as the most controversial specific learning disorder. This condition was first reported in 1896 by a British general practitioner, W. Pringle Morgan, [99] as "A Case of Congenital Word Blindness." Morgan wrote:

> Percy F.—a well-grown lad, aged 14 . . . is the eldest son of intelligent parents, the second child in a family of seven. He has al-

> ways been a bright and intelligent boy, quick at games and in no way inferior to others of his age. His greatest difficulty . . . his inability to learn to read . . . is remarkable, and so pronounced, that I have no doubt it is due to some congenital defect. He has been at school or under tutors since he was seven years old, and the greatest efforts have been made to teach him to read, but in spite of this laborious and persistent training, he can only with difficulty spell words of one syllable . . . The schoolmaster who has taught him for some years says that he would be the smartest lad in the school if the instruction were entirely oral . . .

Many other case reports appeared during the next few decades, especially by ophthalmologists, who were often the first physicians consulted about failure to learn to read.[36] In the first monograph on this subject, published in 1917, James Hinshelwood, a Scottish eye surgeon, reviewed his personal series of 31 cases gathered over a period of nearly 20 years. Hinshelwood regarded this as a relatively uncommon hereditary defect "occurring in children with otherwise normal and undamaged brains."[67]

The first comprehensive study of neurological and psychiatric aspects of specific reading disability was made by an American, Samuel T. Orton. In his classic monograph, published in 1937, Orton emphasized the relationship of reading disability to other developmental language disorders, congenital dyspraxia, and ambiguous or confused handedness.[101]

Following Orton's studies, Paul Schilder and Lauretta Bender developed the concept that developmental dyslexia is a manifestation of disturbed Gestalt function and an accompanying lag in cerebral maturation.[10,12,115] More recently, Drew reported an intensive neurological evaluation of three dyslexic individuals in one family. His findings suggested that parietal lobe involvement was the anatomic substrate for a general disturbance in Gestalt function.[39]

Several extensive medical studies by Scandinavian workers, particularly those by Skydsgaard,[126] Hallgren[63] and Hermann,[66] emphasized the essentially "pure" or specific nature of developmental dyslexia, which they regarded as an hereditary nosological entity. Hallgren concluded from a clinical study of 276 cases the specific dyslexia follows a monohybrid autosomal dominant mode of inheritance with almost complete manifestation.

Since the pioneer multidisciplinary research report on reading disorders in 1954 by Ralph Rabinovitch and his colleagues at the University of Michigan,[109] there has been rapid growth of interest in medical research in this field. Within the present decade, President John F. Kennedy's vigorous leadership and concern over mental retardation marked the start of a new era of public involvement.[103]

An enormous amount of evidence has accumulated, relating learning disorders to linguistic, perceptual and other developmental neurological functions.[37,54,90,97] However, despite this growth of knowledge, there has been considerable resistance to the acceptance of neurological factors as etiologically significant.[106] Conversely, other investigators have extended neurological theory beyond established boundaries to provide rationalizations for faddist remedial techniques.[90,97]

Additional diagnostic perplexity has arisen from the multitude of terms used in various national, state, and local school programs to designate special classes for children who are classified as "educationally handicapped" (EH), "neurologically handicapped," (NH) "perceptually handicapped," or "mentally exceptional."

Many educators and psychologists have opposed all medical concepts of learning disorders, and have resisted the use of terms with medical implications, such as congenital word-blindness, specific language disability, strephosymbolia, developmental dyslexia, and minimal brain dysfunction. Their objections include (1) an unwillingness to consider any hypothesis which relates "milder" learning disorders to cerebral dysfunction; (2) failure to find proof that developmental dyslexia exists as a pure nosological entity affecting any substantial number of children; (3) failure to find any differences between dyslexic children and normal readers in the types of errors made in reading; (4) the great variation in frequency of reading disability in different classes; (5) the usual concurrence of reading disabilities with other defects, and (6) the belief that reading and other language disabilities "should be regarded as phenomena which fall within the framework of normal variation."[86]

Recognizing this controversy, Shankweiler[118] recently wrote:

> Developmental dyslexia clearly should not be regarded as a unitary condition. Just as there are a number of acquired cerebral syndromes in which dyslexia is a prominent symptom, developmental syndromes occur which include reading disabilities of varying

degrees of purity. Developmental dyslexia is necessarily a rather broad concept which refers to a number of types of reading disability which may or may not be related in etiology and in the underlying disturbance of function. The term "developmental dyslexia" is worth retaining, because it refers to a group of disorders which are profitably to be distinguished from the mass of cases of reading backwardness. Clearly, a careful delineation of the various dyslexia syndromes is of the greatest importance for treatment. At present there is little solid knowledge of any of these syndromes and only hints as to ways in which different types of reading disability are linked to salient features of development.

At its meeting in Dallas in April 1968, the World Federation of Neurology's Research Group on Developmental Dyslexia and World Illiteracy, under the leadership of Dr. Macdonald Critchley, formulated and unanimously approved the following definitions:

> 1. *Specific Developmental Dyslexia:* A disorder manifested by difficulty in learning to read despite conventional instruction, adequate intelligence, and socio-cultural opportunity. It is dependent upon fundamental cognitive disabilities which are frequently of constitutional origin.
> 2. *Dyslexia:* A disorder in children who, despite conventional classroom experience, fail to attain the language skills of reading, writing, and spelling commensurate with their intellectual abilities.[134]

In addition to developmental dyslexia, other specific learning disorders are related to deficits in other symbolic functions and intellectual capacities, such as directionality, space-time perception, abstract conceptualization, attention span, and impulse control.[33] Specific writing disability (dysgraphia) may be a practically isolated type of motor deficit, although it often is part of a more diffuse "clumsy child syndrome," or a "congenital dyspraxia."[62] Most cases of "specific" learning disabilities show mixtures of such deficits. Each child presents a unique pattern of symptoms and a complex mixture of relative weaknesses and strengths.[32]

Neurological Studies

During recent years considerable effort has been devoted to the development of more refined techniques for the neurological examination of children with learning and language disorders.[36] Many reports have described the possible diagnostic value of various equivocal or *"soft" signs,* which are often found in these cases in an expanded neurological examination.[4,19,27,31,38,123,124,125] There is need for further standardization and evaluation of many of these equivocal but apparently useful techniques. Some of these "soft" signs include an isolated pathologic toe sign, reflex asymmetry, mild ataxias, tremors, clumsiness, mild hearing defect, and abnormality of extraocular movements. Several of the older neurological tests of higher cerebral function have also recently been studied more intensively in children with learning disorders. These include:

- Synkinesis, also known as abnormal associated movements, mirror movements, or adventitious overflow movements[1,30,47]
- Arm extension test[27,121,125]
- Head rotation test[27,121]
- Dual simultaneous sensory testing[13,78,144]
- Imitation of gestures[17]
- Right-left orientation[9,14]
- Finger identification and localization[14,75,76]
- Choreiform syndrome[93,107,112]

A recent study in England on the visuo-motor abilities of 810 healthy school children brought to light 54 cases (6.7 percent) in which performance was so deficient as to suggest a specific developmental failure. The children with visuo-motor impairment were significantly inferior to controls in a series of tests of spatial judgment and manual skill; they showed a variety of educational problems, especially in spelling and arithmetic. This carefully conducted study supports the view that agnosic-apraxic disabilities in otherwise normal children are "by no means rare and warrant wider recognition."[20]

One-half or more of children with learning disorders reported in various studies have shown significant electroencephalographic abnormalities.[8,31,72] Focal dysrhythmia, especially parieto-occipital, is common. In other cases the dysrhythmia is more diffuse. Obviously, a diagnosis of a learning disorder cannot be made from the electroencephalogram, and a normal electroencephalogram does not rule out a learning disorder.[2,6,58,71,140]

The value of the electroencephalogram in these conditions lies in (1) providing more complete evaluation of the nervous system, (2) confirmation of the "organic" nature of the learning disorder in some instances, (3) ruling out a hidden seizure disorder, (4) providing a baseline for future reevaluation, and (5) better insuring the safety of a trial of activating medications which may at times precipitate seizures (for example, deaner, phenothiazines).

Minimal Brain Dysfunction

Recently the term *minimal brain dysfunction* has been more or less officially adopted in this country for a large group of borderline problems of children, including specific learning disabilities, as recommended in a study sponsored by the National Institute of Neurological Diseases and Blindness.[26] Within this one general category there are included numerous patterns of intellectual, perceptual, conceptual, linguistic, sensory, motor, and behavioral difficulties. This diagnosis has its basis in the demonstration of one or several of these patterns.

There has been considerable opposition to this term, both from within and outside the medical profession, because of the very large variety of symptoms and signs which may lead to its use as a wastebasket sort of label.[59,85] However, in its generality and stress on *dysfunction,* rather than on *disease,* this designation has the great advantage of indicating the need for special help, and still avoiding the branding of a child as "organically damaged."[6] The term may be properly used for some children whose dysfunctions stem from largely social or psychogenic difficulties, as well as for those with borderline organic disorders of the brain.

When appropriately used, the term *minimal brain dysfunction* carries the implication of a relatively minor, hidden type of difficulty.[28] Unfortunately, it has been frequently confused with the older terms, *minimal brain injury* and *minimal brain damage,* which were formerly applied to the same types of problems. In contrast to the older terms, this newer designation implies flexibility, remediability, and a generally favorable prognosis.[26,28]

Cruickshank noted a possible hazard of these labels: " . . . the use of the word 'minimal' frequently serves to minimize the problem in the minds of parents or to place it on a level of less seriousness than it deserves. In reality these children present the most complicated of all learning and adjustment problems . . . There is nothing minimal about any brain dysfunction."[37] It is also important to realize that any misdiagnosis or misunderstanding of this type of problem can have potentially serious long-term implications for the child and his family.[40,41,42]

Any form of deviant maturation in children has a strong tendency to produce anxiety.[21] Common defensive reactions against such anxiety include (1) attention-getting, hostile or aggressive behavior, (2) tics and other compulsive habits, (3) apathy, disinterest, daydreaming, withdrawal from social activities, bizarre attitudes, and autistic trends, (4) regressive phenomena such as recurrence of enuresis, (5) physical complaints, hypochondriasis, and somatization reactions.[53,68,117,119,120] Any of these reactions may be the first indication for the parents to consult a physician about a learning problem.

However minimal, any grade of cerebral dysfunction is accompanied by some degree of ego weakness.[11] Many terms have been used to describe the deficiency in ego development or identity formation which generally occurs in children with learning problems: inferiority complex,[101] pseudoneurosis,[80] impaired self-esteem, poor self-image, self-hatred,[113] and others. An understanding of the nature of this ego weakness is essential for proper management of the entire learning disability.

Hyperkinetic Behavioral Syndromes

One of the most common difficulties in management is the hyperkinetic behavior syndrome, also called impulse control deficit, Strauss syndrome, and other terms. In this condition various degrees and combinations of motor restlessness, impulsivity, distractibility, short attention span, emotional liability, and outbursts of temper may occur.[116,122]

This type of behavior is often erroneously regarded as entirely psychogenic—hence, the recent designation *pseudoneurosis*.[80] However, in most instances, hyperkinetic behavior probably reflects an imbalance in the functional relationships of the reticular formation of the brain stem with the limbic system and neocortex.[105,127] Correction of this anatomical-functional imbalance probably is the basis for the frequently observed paradoxical quieting and stabilizing effects of stimulant drugs.

Psychiatric Studies

Most children with learning disorders show indications of emotional or behavioral reactions, both as a result and a complication of their failure to learn. In some instances these reactions are so severe that the entire complex problem may be wrongly considered to be primarily psychogenic. Conversely, in some children the emotional reactions are kept well concealed. In general, the longer the delay in diagnosis and effective help for a milder learning disorder, the greater the effect on a child's personality.[57]

Rabinovitch and coworkers[109] contrasted the differences in emotional reactions and therapeutic needs of children with different types of reading disability. Those cases classified as "primary reading retardation," based on a hidden neurologic deficit, show prominent anxiety and guilt about the reading incapacity itself. Children with "secondary reading retardation," based on exogenous factors, tend to show a wider range of emotional and behavioral problems, with their major anxieties centered on other problems and not mainly around school adjustment.

Failure to recognize the possible neurological background of a learning problem in a child with minimal brain dysfunction may lead to more serious psychic trauma, to which the child is already predisposed because of a coexistent lowered emotional threshold.[11] Another serious problem is the common inability of parents to recognize and secure early help for the secondary emotional symptoms which follow upon school failure and social rejection. Often, the child's most urgent need is to have a suitable opportunity to achieve some degree of real academic success as soon as possible.[97,98,131]

In certain children, passive-aggressive behavior patterns present one of the most serious and treatment-resistant problems leading to underachievement, despite average or superior intellectual endowment. These patterns generally reflect difficulties arising from complexities of interaction between the child and his parent, often aggravated by pressures at school.[85,110] In some cases other complex problems in family psychopathology operate as causative or complicating factors in learning disorders.[45,87] Failure of a specific remedial educational program may result from a severe family problem, in which one parent, usually the father, is found to be a borderline psychotic whose social stability is preserved by the family's actions to maintain the status quo; the child's refractoriness to treatment is tied to his role in the family—a pseudostupid or infantile subidentity.[95]

Early psychoanalytic writers stressed the importance of psychogenic factors in some cases of reading disability, implicating early traumatic incidents with later anxiety and guilt over unconscious scoptophilic-coprophagic-phallophagic phantasies, regressive gratification of genital impulses, and ambivalance about compulsive exhibitionistic-voyeuristic activity.[3,18,128,130] Even as late as 1960 Anthony stated, "In general, most psychoanalytic authors agree that a regression to a sexualized and aggressivized mode of energy is characteristic of learning problems."[5]

While formulations in such terms may not be generally useful, there is no question that optimal levels of sensory and perceptual stimulation in very young children have great importance for the future development of language skills, problem solving, and other cognitive functions. Early distortions in the child's personality development related to maternal deprivation and other disturbed family relationships often lead to serious impairment in future learning abilities, as well as behavior disorders, psychopathic traits, and psychophysiologic derangements.[23]

Such factors influence every therapeutic program for children who have had any appreciable degree of early personal deprivation, whether determined mainly by cultural and economic factors or by intrafamilial problems. Special difficulties presented by linguistic and motivational barriers to academic achievement in culturally deprived children, even in the earliest school years, also reflect attitudes which are likely to influence psychotherapy and other phases of medical treatment.[102]

Diagnosis: the Interdisciplinary Team Approach

There is no single neurological pattern which is diagnostic of a learning disorder. Indeed, a learning disorder of any type, from a specific developmental dyslexia to a severe global mental retardation, may occur without any clear-cut abnormalities in the standard neurological examination.

An accurate diagnostic formulation of learning disorders requires consideration of multiple factors—social, educational, pediatric, psychiatric, neurologic, psychologic, and linguistic. It is essential that any physician consulted about a learning problem understand, first, the limitations of his own abilities and, second, the potential value of securing other help, both in diagnosis and therapy, from those in other medical specialties and in the cooperating professions.

An interdisciplinary group for comprehensive diagnostic study, and for the formulation and carrying out of a treatment program, may include various specialists in family practice, pediatrics, psychiatry, neurology, ophthalmology, otolaryngology, psychology, education, speech pathology and linguistics, social service, occupational therapy, physical therapy, and nursing. A "minimal" interdisciplinary team for learning and language disorders would consist of a physician, a psychologist, a speech pathologist and a teacher.[51]

As a member of an interdisciplinary team, a physician must set aside, to some extent, his traditional role as an absolute authority on diagnosis and treatment. He must recognize and be able to make proper use of the unique training and frequently superior skills of the other members of the team.[133,136]

Modern psychological testing, using a variety of standardized tests, provides the most refined diagnostic study of many of the highest cerebral functions, usually far beyond the range of the most extended study by a neurologist or psychiatrist. Similarly, the special evaluations carried out by a speech pathologist and an educational consultant provide detailed assessments of other complex functions of the nervous system. The examinations made by these specialists, who often overlap in their interests and skills, are essential to the diagnostic study and remedial planning for a child with a learning disorder.[26]

Treatment: Psychotherapy

All non-educational types of treatment for learning disabilities are merely adjunctive or auxiliary to a remedial educational program, which is designed to help the specific cognitive deficits of an individual child. Psychotherapy is not a specific form of treatment for learning problems, except for those relatively uncommon cases in which the learning difficulties appear to be largely psychogenic.[82]

A careful explanation about the nature of a child's learning problem usually has great value to the child and to his parents and often to his teacher, as well.[60] Any indications of limited grasp due to severe anxiety, denial mechanisms, and other problem attitudes should suggest the need to provide further guidance or other psychotherapy for the child and his family. More extensive psychiatric evaluation is also indicated whenever a child's behavioral difficulties and symptoms continue despite educational and other environmental help.[56,102]

Psychotherapeutic help in many cases may be appropriately limited to practical counseling or guidance for the parents. In most instances parents should be advised to provide an orderly, carefully planned, predictable schedule of home activities in a setting of consistently firm and fair discipline with definite limits of permissiveness, accompanied by kindness, understanding, helpfulness, and encouragement.

Whenever necessary, parents should have help in developing general guidelines and in planning the details of physical activities, recreation, and periods of rest. Usually, the physician should confer with the child's remedial teacher, school psychologist and other consultants before making specific recommendations to the parents about educational matters, such as advice about securing home tutoring or referral to a special school or clinic.

The preliminary planning should consider every available type of standard therapy which might improve the child's total functioning. In most cases, any indicated psychotherapy, drugs, and physical exercise programs can be advantageously used in combination during any phase of remedial education. More rarely, some preliminary period of psychiatric intervention (psychotherapy or drug therapy or both) may be necessary before a child can participate adequately in a remedial educational program.[52]

Ideally, each portion of a "total push" program enhances the efficacy of all of the other means which are being used simultaneously. However, in some cases, too full a schedule may exhaust the energies of children and their parents. No form of treatment, however valuable, should be allowed to take away energy which is more urgently needed for other activities.[74] A hierarchy of treatment needs and values must be established and periodically reviewed in every case.

In some older children and adolescents more time and attention may appropriately be devoted to some form of direct psychotherapy with the child himself. But in every case the parents should also be involved in varying degrees. Other briefer supportive and interpretive forms of therapy may be considered in many instances. For some families a conjoint approach may be useful.[48,102]

Most children with learning problems and their families derive considerable emotional support from the continuing interest and availability of their family physician. This continuing relationship provides for prompt help, whenever needed, over an extended period.[52]

Motor and Perceptual-Motor Therapies

Several programs which emphasize training in body control and visual perception are currently in wide use for children with learning disorders. The methods advocated by Kephart, Getman, and Delacato use a number of similar techniques but with wide differences in theoretical bases.

Kephart's method for developing basic "motor generalization" is supposed to promote perceptual accuracy.[72,73] Getman believes that deficiencies in various visual functions are the basis of learning difficulties; he combines visual training and general motor training.[55]

The Doman-Delacato group believe that children with learning disorders lack "neurological organization." Their training methods aim at a patterned recapitulation of the phylogenetic-ontogenetic stages of locomotor development. They emphasize the use of measures to establish complete unilaterality of motor dominance for eye, hand, and foot, in the belief that these will accelerate and stabilize the localization of language functions in the dominant cerebral hemisphere.[50]

All of these methods may have some value to some children with impaired motor and visual motor skills. The possibility that certain features of these methods may have particular value in some cases requires careful study. However, there is no clear evidence that any of these techniques has any specific educational value for the cognitive functions of children with learning disorders.

There has been considerable concern over the claims of the Doman-Delacato supporters for their theories and techniques which are not consistent with accepted neurological principles.[50,138] Such a complex regimen may be potentially harmful to an individual child and his family when indiscriminately applied, especially in the place of more specific remedial educational techniques.[138] In 1968 twelve major health organizations in the United States of America and Canada concurred in a statement opposing the Doman-Delacato method.[92]

In addition to the Getman program, many other orthoptic and optometric treatments are being used for children with learning disorders.[64] While eye muscle imbalance, convergence difficulties and refractive errors may contribute to learning problems, eye conditions are not generally regarded as the major etiologic factors.

That various unorthodox and faddist programs for children with learning disorders have had such rapid growth and wide use reflects a possible serious deficiency within the medical profession. Parents and educators have felt a critical need for more specific techniques and active help for children with learning and language disabilities. The longstanding tendency to isolationism of the medical profession and consequent barriers to freer communication with other concerned professions must be quickly broken down.[24,138]

Physicians have a serious responsibility to inform and advise parents and educators about the rationale—the possible value and also the potential harmfulness — of any medically based program proposed for treatment of children with learning disorders, either within or outside the classroom. The relevance of any treatment to each child's specific problems should always be the primary consideration.[90]

Early motor disabilities, even when mild and borderline, often lead to exclusion from play activities of peer groups, giving the child insufficient opportunities and motivation to practice motor skills, and a progressive aggravation of the child's basic deviations from the average motor development for his age.[74]

Children with such borderline motor and visuomotor handicaps may derive considerable help from a carefully planned remedial program designed to improve motor skills, body image awareness, right-left discrimination, and hand-eye interactions.[34,35,37]

Many school systems still do not provide formal physical education programs until the level of junior high school or beyond. And most physical education programs chiefly provide an opportunity for the practice and improvement of motor skills already developed outside of school. Fortunately, some school systems are providing more ideal individualized remedial physical educational programs for children with borderline motor handicaps which complicate other learning problems. Physical therapists, occupational therapists, and physical educators with special interest and training can give considerable individual help to children with such difficulties. Physicians should have greater awareness of the general need for improved programs in physical education.[35]

Cerebral Dominance

Treatments such as the Doman-Delacato method and some optometric programs which emphasize motor activities and other measures, such as eye occlusion, designed to influence cerebral dominance, have no sound theoretical basis for the general treatment of learning disorders.[97,138]

The entire problem of cerebral dominance is far more complex than previously believed. It is now recognized that the left cerebral hemisphere is dominant for language functions in many, probably a majority, of left-handed persons as well as in right-handers.[91,100,129,141,142]

While anomalous handedness and mixed or confused eye-hand preference frequently occur in children with learning disorders, these do not have any cause-effect relationship.[9,141] It is well known that similar patterns of confused or mixed motor laterality occur in the general populations with great frequency.[138]

Handedness exists in many gradations; estimates of the incidence of left handedness vary from 1 percent to 30 percent in different studies, using different criteria and examination techniques.[65]

Cerebral laterality for handedness and language are not directly linked, and one does not determine the other.[91] Exercises and eye treatments which are designed to change laterality of motor skills cannot be expected to provide an effective basis for the specific treatment of a child with a complicated deficit in perceptual and other cognitive abilities.

Drug Therapy

Drugs have only relatively limited usefulness in the broad field of learning disorders.[49] However, in certain cases the proper use of a specific medication can be of great value in controlling behavioral symptoms which interfere with learning.[43,46]

The cerebral stimulant drugs have been shown to have a paradoxical calming effect on hyperkinetic behavior. Either dextro-amphetamine (Dexedrine®) or methylphenidate (Ritalin®) may be effective when used in proper doses. These drugs may also be helpful for some children who have a short attention span or difficulty in concentration but are not otherwise hyperkinetic. Deanol (Deaner®) is a more controversial stimulant which may be of value in some cases.[96,137]

Barbiturates and mild tranquilizers of the propanediol series, such as meprobamate (Miltown®), have generally less value in these problems and may actually have an undesirable paradoxical stimulant effect.

In some more severe forms of hyperactivity, especially when accompanied by more bizarre, negativistic, aggressive, schizoid or autistic behavior, one of the major tranquilizers of the phenothiazine series may be useful. Here the choice generally lies between a more sedative agent such as chlorpromazine (Thorazine®) and thioridazine (Mellaril®) and a more stimulant drug such as trifluoperazine (Stelazine®) or fluphenazine (Prolixin®, Permitil®).

Other drugs which have been advocated for hyperkinetic behavior disorders include diphenylhydantoin sodium (Dilantin®), diphenhydramine (Benadryl®), hydroxyzine (Atarax®, Vistaril®), chlordiazepoxide (Librium®), and diazepam (Valium®). Anticonvulsants, such as diphenylhydantin (Dilantin Sodium®) and primidone (Mysoline®), may best be reserved for use when a subclinical convulsive disorder is suspected.

In younger children with enuresis the tricyclic (iminodibenzyl) antidepressants, such as imipramine (Tofranil®) and nortriptyline (Aventyl®) are frequently quite valuable, both in providing fairly prompt bladder control and in helping classroom behavior. Older children and adolescents who have depressive trends also may be helped by tricyclic agents.

The dosage of any of these drugs should be individually adjusted, usually starting with small doses and increasing as rapidly as possible to the optimal effective level. Adequate arrangements should be made in every case to assure appropriate observations and medical supervision. Physicians may advantageously use the help of teachers and school nurses, both in administering a midday dose of medication and in observing the effects of a drug on the child's behavior in a variety of situations at school.[83,135]

Many physicians disapprove the use of psychotropic medications for behavior disorders, on the ground that the prescription of drugs might be misinterpreted by parents or teachers and brand the child as "organically damaged." Others, especially psychiatrists, have viewed drugs as potentially antipsychotherapeutic.

Drugs obviously cannot take the place of necessary remedial education, psychotherapy or environmental changes. However, appropriate drug therapy may facilitate any needed psychotherapy or special educational program. Postponement or refusal of a trial of indicated medication in behavioral syndromes complicating learning disorders can be an unwarranted barrier to prompt relief of symptoms which block learning.

Conclusion

Through his broad knowledge of higher cerebral functions and their complex relationships with general physical and mental health, the physician is in the best position to help parents understand their child's learning problem and to secure their cooperation in arranging for any necessary remediation. The physician is also the appropriate person to provide the general public, including legislators and school administrators, with sound information on the medical aspects of learning problems.[29]

The physician has a major responsibility to provide the leadership in the development of team programs, to help integrate diagnostic and therapeutic procedures, and to work vigorously toward providing earlier and more complete help for children with learning disorders.[42,52] It is clear that if the physician cannot play a leading role, these problems will be dealt with by those less competent to do so.[90]

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ALPHA-TOCOPHEROL TO FORFEND THROMBOSIS

"About 19 years ago, a young man at our institution did some work on blood coagulation. He showed that alpha-tocopherol in the presence of calcium exerts an antithrombic effect. In the last 18 years, I have been using this routinely in all patients in whom I've done major surgical procedures. And in the 18 years that I've been using this routinely and immediately after operation, I've had one case of pulmonary embolism. I thought this was the one failure. But autopsy showed that the man's embolus came from his atrium, and not from his peripheral arterial system. He had it at the time we operated on him. So I think that this is a real worthwhile drug. The advantage of it is that although it decreases the thrombic activity, it doesn't increase the bleeding tendency. We use 100 international units, three times a day, given parenterally first and then by mouth."

—ALTON OCHSNER, M.D., New Orleans
Extracted from *Audio-Digest Surgery,* Vol. 15, No. 24, in the Audio-Digest Foundation's subscription series of tape-recorded programs.

Ocular Findings in Several Metabolic Diseases

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■ *Changes in ocular findings have been noted in association with several metabolic diseases.*

In homocystinuria the crystalline lens in the majority of cases is subluxated inferiorly, while in Marfan's syndrome the dislocation was upward.

In cystinosis, slit-lamp examination reveals numerous gold crystal-like cystine deposits in both the cornea and bulbar conjunctiva.

Patients with galactosemia have cataracts of the "oil drop" type, which usually can be seen with an ophthalmoscope even though the opacity is not dense.

Eight patients with Lowe's syndrome who were observed had cataracts, and four of them had severe glaucoma.

Three of five patients with glycogen storage disease Type I had yellowish deposits in the macular and paramacular areas, thought to be due to hypercholesterolemia.

MANY PHYSICIANS do not realize the extent to which ophthalmologic findings are associated with defects of metabolism. Although these conditions are rare, there is always a good possibility that an ophthalmologist will encounter one or more in the course of his practice. The entire scope cannot be covered here, but several metabolic diseases and syndromes studied by the author will be discussed. The entities to be considered are homocystinuria, Marfan's syndrome, cystinosis, galactosemia, Lowe's syndrome, and glycogen storage disease, Type I.

Homocystinuria

Homocystinuria,[1] a disorder of amino acid metabolism, was first described in 1962. It begins in infancy. Patients have a malar flush, fine hair and congenital anomalies. Mental retardation and dislocation of the crystalline lenses are the chief findings. Many of the patients die, due to thrombosis of major vessels. The physical characteristics of these patients resemble those seen in Marfan's syndrome, a different metabolic problem in which there is cardiac disease but no thrombosis of the vessels. The diagnosis of homocystinuria is made by finding homocystine in the urine. In this disease the subluxation of the crystalline lenses is downward; in Marfan's syndrome, it is upward.

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Presented before the Section on Ophthalmology at the 98th Annual Session of the California Medical Association, Los Angeles, March 15 to 19, 1969.

Reprint requests to: 1127 Wilshire Boulevard, Los Angeles, Ca. 90017.

Cystinosis

Cystinosis,[2] or Lignac-deToni-Fanconi syndrome, is a systemic disease of unknown cause. The generalized amino-aciduria and renal glycosuria associated with this condition are clues to the diagnosis. Rickets is a consistent finding and the patients have been sometimes called nephritic dwarfs. Death frequently occurs during the first ten years of life due to renal insufficiency. Depositions of cystine crystals occur in various tissues. These crystals are easily visible with the slit-lamp in the stroma of the cornea, appearing as myriads of fine gold flakes. They probably account for the photophobia which is a common complaint. The crystals are also present in the conjunctiva. By ophthalmoscopic examination alone, the cornea may be completely clear, and the diagnosis thus may be missed. Cystinosis should not be confused with cystinuria.[3] Cystinuria is inherited as a recessive disease which is characterized by the frequent formation of cystine urinary calculi as the most important clinical finding.

Galactosemia

Galactosemia[4] is an inborn error of carbohydrate metabolism. There is a deficit in the activity of a specific enzyme, galactose-1-phosphate uridyl transferase. Infants with galactosemia appear normal at birth and do well until milk feedings are begun; then certain symptoms such as fever, vomiting, inability to gain weight and, at times, diarrhea occur. Jaundice and hepatomegaly are consistently found, and splenomegaly occasionally. Ascites may occur. It is important to diagnose the condition at this stage because most of the symptoms and findings can be reversed by prescription of a lactose-free diet. If untreated, the surviving infants develop cataractous changes and mental retardation. The diagnosis is suspected on clinical grounds and strengthened by the finding of a reducing substance (galactose) in the urine. The usual test using Benedict's solution produces a positive reaction, but there is a negative reaction when glucose oxidase is used. The diagnosis is now confirmed by the absence of transferase enzyme activity in red cells. The enzyme activity is nil or almost nil in the hemolysates of patients with galactosemia, and the activity is reduced in carriers.[5,6]

The evolution of the genetics of galactosemia took years of study before Kirkman and Bynum[5] and Donnell, et al[6] established that the inheritance of the disease is as an autosomal recessive. It is extremely important in genetic counseling to warn the parents that subsequent babies may have the same disease. The risk is one out of four in each future pregnancy.

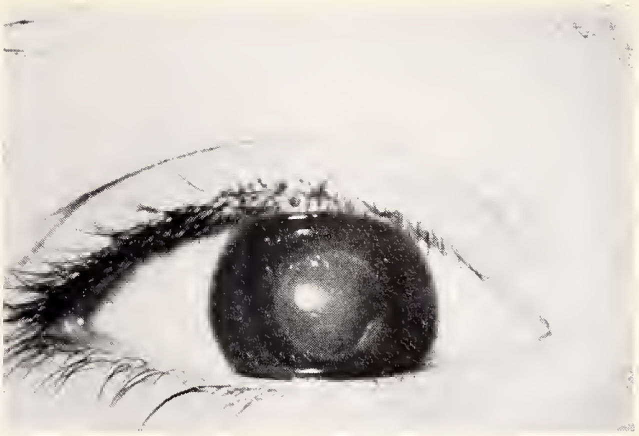

Figure 1.—Galactosemic cataract with surgical coloboma.

In the last 20 years, 45 patients with galactosemia have been examined and treated at the Children's Hospital of Los Angeles. The author has had the privilege of examining the eyes of all of these patients and of following them periodically. Cataract is the main eye defect associated with galactosemia; it was present in 42 percent of the patients. It is suspected that the changes in the crystalline lens are due to accumulation of galactitol, an end-product of an alternate galactose pathway.[7] These cataracts have often been referred to as the "oil drop" type (Figure 1) because of their appearance upon examination with the ophthalmoscope. Biomicroscopic examination reveals cloudy changes in the embryonic and fetal nuclei and there may be fine radiations extending out in the posterior cortex. About two-thirds of the central area is usually involved. The peripheral cortex may remain quite clear. Interestingly, over the years, operation for removal of galactose cataracts has been done in very few cases. The author reported performing optical iridectomy on one of our first patients.[8] In this case, the diagnosis was not made until the infant was seven months of age, and the cataracts had much more time to develop.

Sometimes there are no opacities whatsoever in the crystalline lens. In most of the cases diagnosed during the first month of life the opacities have been minimal. It has been reported that galactose cataracts will completely resolve with dietary treatment, but in our experience some minimal opacity

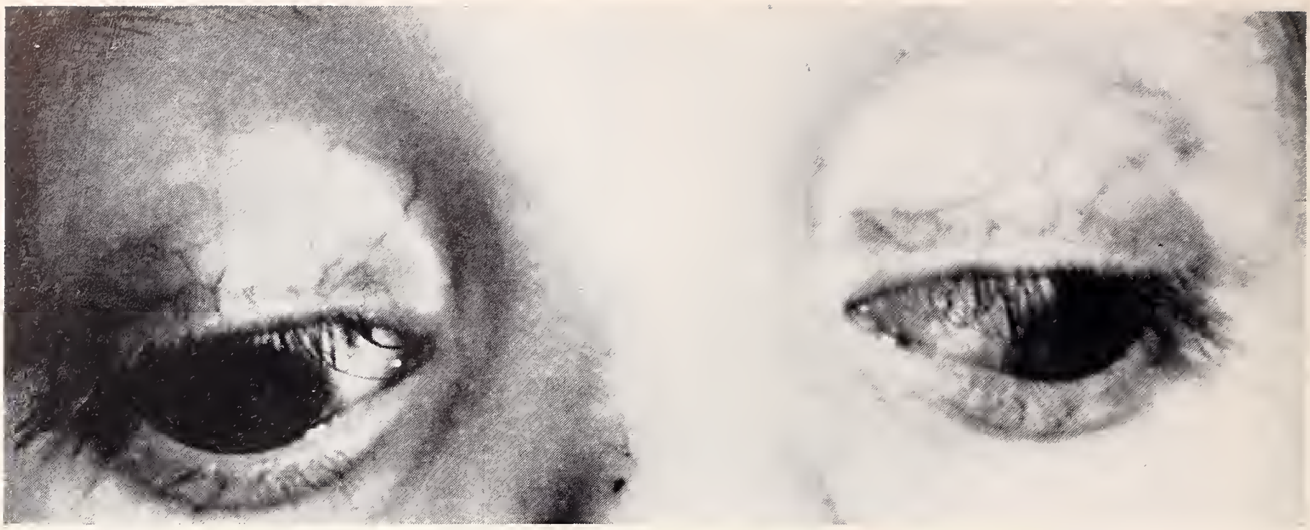

Figure 2.—Lowe's syndrome. Corneas cloudy from glaucoma. Cataracts present.

remains in the crystalline lens even though there is regression of the cataract.

It is stated in the literature that cataracts do not occur in patients less than one month of age. However, we had one patient who was diagnosed as having galactosemia at two and a half weeks of age and the opacities were quite advanced and easily seen on ophthalmoscopic examination. The lens changes almost entirely regressed in this case after the patient began receiving a prescribed diet.

Opacities of any kind in the crystalline lens may cause some impairment of vision. In the patients we have observed over a period of many years, it has been found that the eyes do not always have 20/20 acuity, but useful vision is usually present.

Lowe's Syndrome

The oculo-cerebral-renal syndrome of Lowe[9] is a relatively new disease, first described in 1952. This is a congenital and inherited condition manifested by defects of the nervous system, the eyes and the kidneys. Laboratory tests disclose proteinuria and hyperaminoaciduria.

Eight cases seen at the Children's Hospital were reported in 1963.[10] All the patients were male, were short of stature, were severely mentally retarded and had cataracts. Four had congenital glaucoma as well (Figure 2). Seven of the eight had bilateral cryptorchidism.

The cataracts varied from partial to total involvement of the crystalline lens. The four with glaucoma perhaps should have been listed as having hydrophthalmos, for the condition was present at birth and was characterized by pronounced edema of the cornea and by high intraocular pressure as determined by tonometer with the patient under anesthesia. Operation for glaucoma in these cases was basically limited to iridencleisis because the corneas were not clear enough for the performance of goniotomy. In a few cases, goniotomy was performed as a secondary procedure when the corneas were clearer. Complete control of the intraocular pressure was not satisfactory, and the cataract operation was only partially successful. Because of the mental retardation, it was impossible to determine visual acuity in these patients, nor was it possible to tell whether or not they were deaf. The cataract operation was either linear extraction or aspiration. All patients had some posterior capsular remnants which precluded an adequate view of the fundus.

The genetic aspect of this disease is extremely interesting. The parents, siblings and grandparents of all of the patients we observed were given a thorough ocular examination. On slit-lamp examination three mothers and one maternal grandmother were found to have partial cataracts. Four mothers had numerous punctate opacities throughout the cortex of the crystalline lens of both eyes. The opacities often had the appearance of snowflakes. Similar changes were present in the crystalline lens in two maternal grandmothers, one maternal aunt and three female children. Based on pedigrees and the fact that all patients are males, Lowe's syndrome is generally considered a sex-linked disorder. The ocular findings described in mothers and female relatives are manifestations of the heterozygous state.

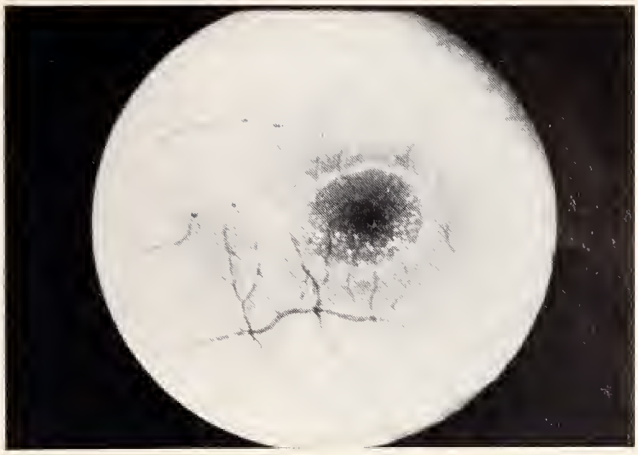

Figure 3.—Macula in glycogen storage disease.

Glycogen Storage Disease

Glycogen storage disease Type I, sometimes referred to as Von Gierke's disease, is a hereditary metabolic disorder manifested by low or absent activity of the enzyme glucose-6-phosphatase in the liver, kidney and small intestine. There is an accumulation of glycogen in these tissues—hence the term "glycogen storage disease." Clinically, the disease is characterized by short stature, massive hepatomegaly, hypoglycemia, lactic acidosis and hyperlipidemia.

Five cases of glycogen storage disease were studied in considerable detail, including complete ocular examination.[11] Three of five patients had multiple bilaterally symmetrical, yellowish, nonelevated discrete paramacular lesions (Figure 3). The media were clear on biomicroscopic examination. The blood vessels and optic discs appeared normal and no lesions were noted in the periphery of the fundus. Changes were striking in one case, less so in the others. There was no visual impairment and no evidence of other ocular disease in any of these patients. The patients had elevation of blood phospholipids, triglycerides, cholesterol and total lipids. The patient with the greatest ocular involvement had the highest levels.

Similar yellowish spots in the macular and paramacular areas have been observed in a number of adults and an occasional older child who do not have glycogen storage disease. In these cases, the blood cholesterol has been decidedly elevated, usually in the 400-500 mg per 100 ml range. In our series of glycogen storage disease patients, only three had elevated cholesterol levels (542, 518 and 315 mg per 100 ml). Cholesterol level were within normal limits in the other two patients. To date, we have no histopathological studies to verify what the tissue changes in the retina may be. Because of the high cholesterol content in the blood and in light of the fact that the yellow spots have been seen also in adults without Von Gierke's disease, it is thought that the changes are due to cholesterol crystals or deposits. A low cholesterol diet in adults who do not have Von Gierke's disease has been reported as reversing the ocular findings. However, in Von Gierke's disease, the cholesterol and other lipids continue to be higher than normal despite low dietary intake.

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CASE REPORTS

Hypogonadotrophic Hypogonadism in Hemochromatosis

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HYPOGONADISM, one of the classic manifestations of hemochromatosis, was studied in two patients with this disorder. The clinical and histological findings in the two patients were correlated with measurements of gonadal and gonadotrophic hormones.

Reports of Cases

Case 1. The patient was a 32-year-old white man who had diffuse skin pigmentation since age 12. His pubic, facial, and axillary hair had always been sparse. His testes had not grown since age 11, but he believed his libido had developed normally. Cardiac manifestations which led to the admission of this patient to hospital have been reported elsewhere.[1]

At admission it was observed that diffuse pigmentation of the skin gave it a slate-grey appearance and it was smooth and hairless. The patient was 76½ inches tall, his arm span was 79¼ inches, crown-to-pubis segment 36½ inches, and pubis-to-floor segment 40 inches. The escutcheon was that of females. The testes were soft and each measured 1.8 cm in maximum diameter, the penis was small and the prostate gland not palpable. Gynecomastia was absent. The liver edge was felt 8 cm below the right costal margin.

The serum iron level was 270 μg per 100 ml and the unsaturated iron-binding capacity was less than 50 μg per 100 ml. Results of a standard oral glucose tolerance test were as follows: fasting blood glucose, 104 mg per 100 ml; one-hour, 218 mg; two-hour, 264 mg; three-hour, 304 mg; and four-hour, 134 per 100 ml. Liver function studies showed no abnormality. Urinary excretion of 17-ketogenic and 17-ketosteroids was within normal limits, as was the response to a standard oral metapyrone test. Results of thyroid function tests were normal. The plasma testosterone level[2] was 0.088 μg per 100 ml (normal 0.3 to 1.1). The levels of plasma luteinizing hormone (LH)[3] and of plasma follicle stimulating (FSH) hormone[4] were each less than 5 milliInternational Units (mIU) per ml (normal 5 to 30).

Biopsy specimens of liver, skin and heart revealed evidence of hemochromatosis. Biopsy sections of a testis (Figure 1) revealed a prepubescent appearance. The seminiferous tubules contained numerous Sertoli cells with only occasional primordial sex cells. An occasional tubule was sclerotic. Iron deposition was noted in some of the Sertoli cells, but not in the scanty stromal fibroblasts. The patient has been treated with weekly phlebotomy, insertion of an epicardial synchronous pacemaker,[1] and fluoxymesterone, 10 mg daily.

Case 2. A 66-year-old father of two daughters, aged 33 and 39 years, had hemochromatosis diagnosed and confirmed by liver biopsy at age 54 in 1954. Insulin-dependent diabetes mellitus was also found then. Since 1954, the patient had been treated with multiple phlebotomy. Liver biopsy sections in 1962 revealed disappearance of abnormal iron staining.

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Submitted 6 May 1969.

Reprint requests to: Assistant Chief, Endocrinology Section, Veterans Administration Hospital, 5901 East Seventh Street, Long Beach, Ca. 90801 (Dr. Kent).

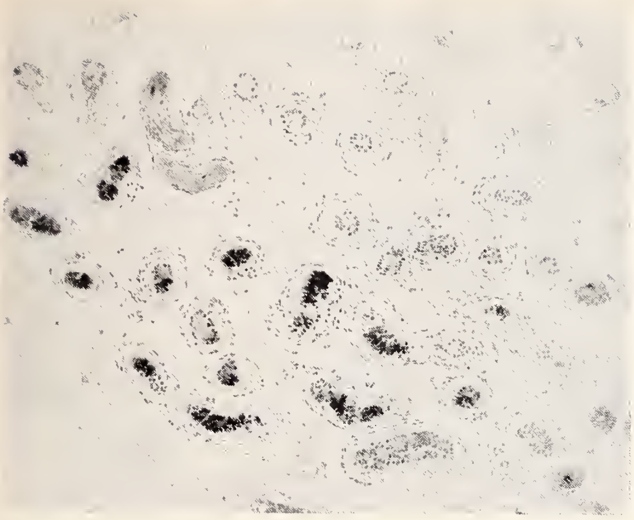

Figure 1.—Section of testis (Case 1). There is immaturity of the seminiferous tubules with an occasional sclerosed tubule, loose stroma, and absence of Leydig cells. Iron deposits are present only in the Sertoli cells. (Gomori's iron reaction, 100X).

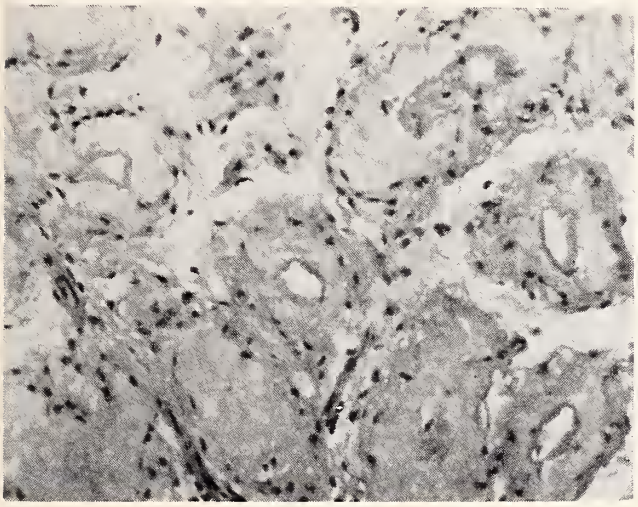

Figure 2.—Section of testis (Case 2). There is pronounced thickening of the seminiferous tubules and absence of spermatogenesis. The Leydig cells are scanty and atrophic. No iron deposits are seen. (Gomori's iron reaction, 300X).

In 1966, the patient had fine wrinkling of the forehead, minimal bitemporal hair recession, and scanty axillary and pubic hair. His testes measured 3 cm in greatest diameter and were soft. The penis was 7 cm long, the prostate gland of normal size. The liver edge was palpable 3 cm below the right costal margin.

Liver function studies were within normal range. The fasting glucose level was 192 mg per 100 ml. Results of thyroid function tests were normal. Urinary excretion of 17-ketogenic and 17-ketosteroids was normal, as was the response to a standard oral metapyrone test. The plasma testosterone level was 0.082 μg per 100 ml. Plasma LH level was low (< 4 mIU per ml) as was plasma FSH content (< 3 mIU per ml).*

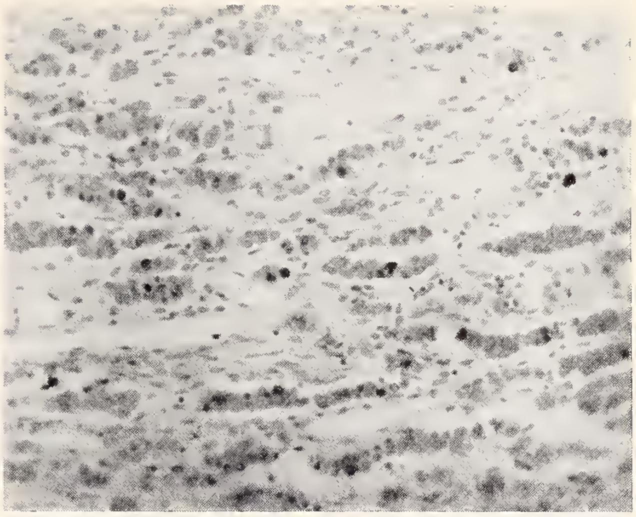

Figure 3.—Section of pituitary gland in Case 2. Numerous iron deposits are seen in all cell types, especially the basophils. (Gomori's iron reaction, 200X).

Biopsy sections of the testes revealed moderate sclerosis of the seminiferous tubules, with spermatogenesis absent (Figure 2). The interstitial cells were sparse and atrophic. No iron deposits were present.

A year after the above studies were performed, the patient died of a primary hepatoma. At autopsy, both testes were atrophic, and no iron deposition was present. There was, however, extensive iron deposition in the pituitary gland, especially involving the basophils but also other cell types (Figure 3). Extensive fibrosis and iron deposition were also present in the pancreas. No abnormal iron deposition was seen in the liver.

Discussion

The findings in both patients are consistent with the diagnosis of hypogonadotrophic hypogonadism.[5-7] The case of the younger patient is a classical example of hypogonadism due to pubertal pituitary gonadotrophin failure. He had eunuchoidal features, clinical and laboratory evidence of androgen deficiency, and testicular histology characteristic of this disorder. He also had low levels of plasma LH and FSH fitting the clinical syndrome of "isolated" hypogonadotrophic hypogonadism recently reported by Hornichter et al.[8] This patient resembled one reported by Althausen and Kerr[9] in whom hypogonadism also antedated puberty and was believed by the authors to be due to a disturbance of pituitary function secondary to iron deposition. Although symptoms develop before age 30 in only 4 percent of patients with hemochromatosis,[10] pituitary gonadotrophin insufficiency was believed to be the cause of hypogonadism in another subject with juvenile onset hemochromatosis.[11]

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*The FSH and LH assays were performed by Albert F. Parlow, Ph.D., Harbor General Hospital, Torrance.

The older patient of the two reported upon herein had the more usual, later onset of gonadal failure. Testicular histology resembled that of a patient with hemochromatosis classified by Albert[12] as typical of adult onset hypogonadotrophic hypogonadism. Also the low plasma FSH and LH together with the low PT are consistent with the diagnosis of hypogonadotrophic hypogonadism and provide evidence against primary testicular failure, in which increased gonadotrophins would be expected.[7,13]

Iron deposition in both the pituitary gland and testes is common in hemochromatosis.[14] Although hypogonadism occurs in some patients with hepatic insufficiency, it is unlikely that testicular failure in the two cases presented can be attributable to liver disease. Hypogonadism, when it occurs in hepatic disease, is usually associated with advanced clinical[15] and morphological[16] stages of hepatic decompensation. In both patients, hepatic function studies were normal at the time of the tests to determine endocrine function.

Until recently, complete pituitary insufficiency had not been documented in hemochromatosis except in rare reports of massive or focal necrosis of this gland.[17] Pituitary iron deposition in the two cases presented here appears to have selectively impaired gonadotrophin function. A recent report, however, demonstrates that deficiencies of other anterior pituitary hormones may also occur in this disease.[18] The present study indicates that impaired FSH secretion as well as impaired LH secretion contributes to the hypogonadism of hemochromatosis.

Summary

Hypogonadism, one of the classic manifestations of hemochromatosis, was studied in two patients with this disorder. The clinical and histological findings were correlated with measurements of gonadal and of gonadotrophic function. Hypogonadotrophic hypogonadism was found in both patients.

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Polymyalgia Rheumatica and Associated Arteritis: A Review

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POLYMYALGIA RHEUMATICA is a syndrome which has been described during the past 15 years, mostly by the English and Scandinavians, but articles have appeared in the American literature with increasing frequency since the first case report in 1963.[1]

It affects middle-aged and elderly persons, infrequently those under the age of 50 years, with women more often afflicted than men. The chief complaints consist of pain and stiffness of shoulder and pelvic girdles, with constitutional symptoms and decidedly accelerated erythrocyte sedimentation rate (ESR) but without significant objective findings or x-ray changes. Generally, the disease runs a self-limited course, with complete recovery occurring spontaneously after several years, but the course may be shortened and morbidity decreased by treatment with corticosteroids.

History

Retrospectively, this syndrome was probably first described by a British physician named Bruce in 1888[2] who referred to "senile rheumatic gout" with severe pains followed by complete recovery. Then no further recognizable reports appeared until 1945 when Meulengracht[3] described "humeroscapular periarthrosis" with fever, weight loss and elevated ESR. In that same year Holst and Johansen[4] spoke of "peri-extraarticular rheumatism" occurring in elderly women and associated with low-grade fever and accelerated ESR. Kersley (1951)[5] described "myalgic syndromes of the aged with systemic reaction" as severe, widespread muscle pain and tenderness of the scapular and thigh regions, with accelerated ESR but without arthritis. Bagratuni (1956)[6] discussed "anarthritic rheumatoid disease," characterized by generalized muscle aches and stiffness, especially in the shoulders, neck and back, with fever, weight loss, anemia, malaise, anorexia, accelerated sedimentation rate, absence of arthritic changes roentgenographically and an excellent prognosis. Barber (1957)[7] described a myalgic syndrome with constitutional effects in 12 patients between 46 and 68 years old, followed for up to seven years, with findings similar to those above, and with a good prognosis. He called this syndrome "polymyalgia rheumatica."

Etiology

The cause of this condition is unknown, but during the past eight years giant cell cranial arteritis has been implicated as the underlying histological lesion by various authors.

Porsman[8] in 1951 was the first observer to associate multiple myalgic pains and aches with temporal arteritis. Paulley and Hughes[9] believed that the myalgias usually precede arteritis by weeks to years. Following up these clues, they performed temporal artery biopsy on 23 patients with both symptomatic temporal arteritis and polymyalgia rheumatica without obvious artery tenderness and swelling and found 21 to have histologic changes of arteritis. It now seems quite clear that the myalgias and arthralgias of giant cell arteritis which present as temporal arteritis can closely mimic the symptoms of polymyalgia rheumatica, and may definitely antedate the obvious vascular changes.[10] Alestig and Barr,[11] on biopsy of asymptomatic

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Supported in part by USPHS Grant No. 05068 and USPHS Grant No. GM15759.

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temporal arteries in ten persons with polymyalgia rheumatica, found giant cell arteritis in seven. They proposed the name "arteritis senilis," based on the ages of the patients, and expressed belief that it is a variant of giant cell arteritis.

Hamrin[12] studied 21 patients with polymyalgia rheumatica, including 12 with asymptomatic temporal arteries, and found giant cell arteritis in 12, of whom six were asymptomatic. Four others showed non-specific inflammatory changes, while the remaining five had normal arteries. It is of interest that in this latter group of five, three had become asymptomatic at the time of biopsy and each of the other two had been symptomatic for less than three months. Hamrin coined the term "polymyalgia arterica" for this condition.

Dixon,[13] on biopsy of temporal arteries in 28 patients with polymyalgia rheumatica, found ten positive for arteritis. He concluded that these conditions represented a single entity. Wilske and Healey[14] expressed the opinion that polymyalgia rheumatica may either precede or follow symptomatic temporal arteritis. Fessel and Pearson[15] advocated early temporal artery biopsy in all cases of polymyalgia rheumatica in order to rule out the presence of giant cell arteritis and its accompanying danger of sudden blindness from ophthalmic artery involvement when untreated.

A few observers have not accepted the apparent relationship between arteritis and the polymyalgic symptom complex. Bagratuni,[16] who referred to the condition as "anarthritic rheumatoid disease," felt that polymyalgia rheumatica more closely resembles the prerheumatoid features of rheumatoid arthritis. He said that rheumatoid arthritis developed in 2 of his 50 patients, and he also was of the opinion there was no relationshp to arteritis. However, he did not perform temporal artery biopsy in any of the patients. Gordon,[17] on the other hand, found no proof that polymyalgia rheumatica was a variant of rheumatoid arthritis and also felt that it was not related to arteritis *per se*. Although his biopsy studies of muscles, synovium and other periarticular structures showed only non-specific infiltration of chronic inflammatory cells, like Bagratuni he did not perform arterial biopsy. Others have found that muscle biopsy is invariably negative, probably because only medium and large sized arteries are affected in giant cell arteritis, whereas such vessels are rarely obtained in routine muscle biopsy specimens.[11,18,19]

In one instance, reactive depression and myalgias of the shoulder and pelvic regions developed during isoniazide treatment for urogenital tuberculosis, after 180 grams had been given over a nine-month period.[20] This condition was followed by polyneuropathy and it was named pseudo-polymyalgia rheumatica. To date this has been the only case to be reported in which the condition was possibly drug-induced.

Whereas some observers[7,12,21] consider polymyalgia rheumatica to be a definite disease, others suggest that it is not a specific disease but rather a symptom complex secondary to a number of unassociated diseases[22] and may be produced by such trigger factors as excessive fatigue and psychological trauma.[23]

Incidence

There is no known racial or geographic distribution. Dixon said that this condition made up 1.3 percent of all cases of rheumatic disease in patients seen in his clinics.[13] He believed it to be more common than ankylosing spondylitis, as common as gout and, at the age of 70 years, one-half as common as rheumatoid arthritis. At a younger age, it was found in a ratio of 1:12 to rheumatoid arthritis. Regarding the relative incidence as compared with ankylosing spondylitis, the latter condition has been seen much less frequently by the English than by physicians in the United States.[24] Many English observers feel that polymyalgia rheumatica is common in elderly people and that the diagnosis is not being entertained.

Symptoms

The old literature described an initial "flu syndrome." Usually the onset of symptoms is quite sudden and patients often remember the exact date and even the hour. The main complaints are pain and stiffness of the shoulder girdles and, somewhat less commonly, the pelvic girdles. Myalgia affects the posterior neck muscles, deltoids, biceps, trapezii, and less frequently the glutei, hamstrings and quadriceps. Pain is worse in the morning and with inactivity. It is also aggravated by motion, especially initially. Swelling is uncommon. There is also less intense pain and stiffness of periarticular structures, including bursae, tendons and sheaths, synovia and capsules.

Constitutional symptoms occur frequently, including fatigue, weight loss, anorexia, sweating, insomnia secondary to pain, fevers lasting for weeks, and depression. Although fevers are usually of low grade (99 to 100°F), one observer[19] noted fevers up to 103°. Intermittent claudication was noted in one instance[22] and pruritus in several others.[2,12]

Physical Examination

Pertinent findings include fever, slight tenderness of muscles and periarticular areas, absence of muscle atrophy (with one exception reported[12]) and mild limitation of motion which varies with pain and is usually of short duration. Tenderness or nodular swellings or both along the course of cranial arteries is often present. Small, asymptomatic effusions of one or both knees were recently reported by Wilske and Healey[14] in 8 of 18 patients. Murmurs were heard over large arteries in 30 of 52 patients studied.[25] Palpable synovial thickening of one or both sternoclavicular joints was observed in 32 of 80 patients.[26]

Laboratory

Mild hypochromic anemia is often present, but with specific treatment for polymyalgia rheumatica or spontaneous improvement the anemia is resolved. The most specific criterion is a decidedly elevated sedimentation rate (Westergren method), often exceeding 100 mm in one hour. All observers agree on this finding. When pain and stiffness abate, or when steroid therapy is begun, the sedimentation rate decreases or returns to normal. Although the leukocyte count is usually normal, there may be mild leukocytosis. The cell differential is generally normal, but slight eosinophilia may occur. One observer noted casts (hyaline, granular) on urinalysis in 4 of 18 patients.[14]

Tests for rheumatoid factor have been negative in all instances, except for Bagratuni's[6] and Bruk's[26] reports of several positive Rose-Waaler tests. One patient with granulomatous temporal arteritis had rheumatoid factor in the lesion but not in serum.[27] Mild decrease in serum albumin and increases in alpha-1 and gamma globulins occur, while there is pronounced increase in alpha-2 globulin. With therapy, these protein changes revert to normal. Serum fibrinogen increases significantly, often to greater than 900 mg per 100 ml. Antinuclear antibodies, LE preparations, calcium, phosphorus, alkaline phosphatase, and muscle enzyme determinations have all been normal. One report of abnormal liver function studies has appeared.[28] Results of electromyography and examination of bone marrow aspirate have always been normal.

Radiography

X-ray changes showing osteoporosis and degenerative arthritis have been noted to be consistent with the patients' age. With the possible exception of Bagratuni,[16] investigators have noted no evidence of active arthritis. Selected angiographic studies have revealed stenosis at the sites where murmurs had been heard over large vessels[25] and arterial narrowing of the major arteries in the lower extremities was also noted in a few cases of polymyalgia.[22]

Pathology

Muscle biopsy, as was noted earlier, shows no evidence of degenerative or inflammatory changes either in the muscle or in the intramuscular vessels. This is probably due to the small caliber of these arteries, whereas the changes of giant cell arteritis occur in medium and large sized arteries. In two patients, however, perivascular infiltrates of lymphocytes were present in muscle septa.[21]

Arterial biopsy has been performed by various investigators, as previously mentioned. In one case with intermittent claudication, there was a panarteritis with pronounced intimal proliferation producing symmetrical narrowing of long portions of the major arteries to both lower extremities.[22] Giant cells were found in the subclavian artery,[25] suggesting disseminated arteritis. At post-mortem examination of three patients who died of other causes after having been followed for up to five years for polymyalgia rheumatica, a disseminated giant cell arteritis of the aorta and some of the great vessels from the aorta were noted.[29] One case of granulomatous myocarditis was found at autopsy.[30]

Most rewarding have been the results of a temporal artery biopsy, already discussed. Microscopically, findings consisted of panarteritis with giant cell granuloma and fragmented elastic fibers in the media as well as intimal thickening producing a narrowed lumen with thrombus formation or intimal swelling (Figures 1 and 2). Negative biopsy may be due to patchy or segmental involvement of arteries, so that specimens might be taken from "skip" areas. Biopsy from other than temporal arteries has shown only non-specific changes.

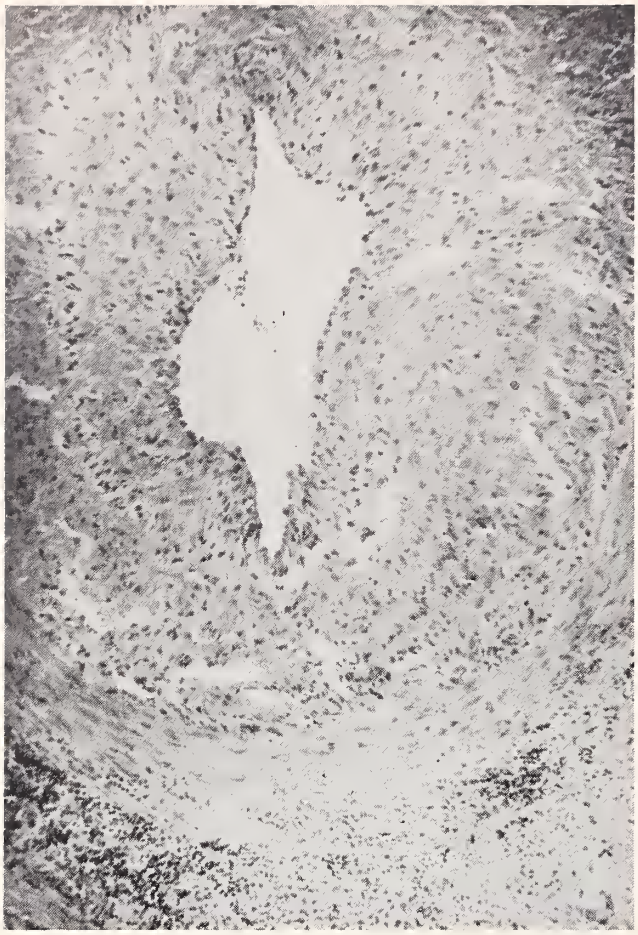

Figure 1.—Temporal artery showing acute arteritis, intimal and medial edema and some inflammatory reaction. Pronounced inflammation in the adventitia.

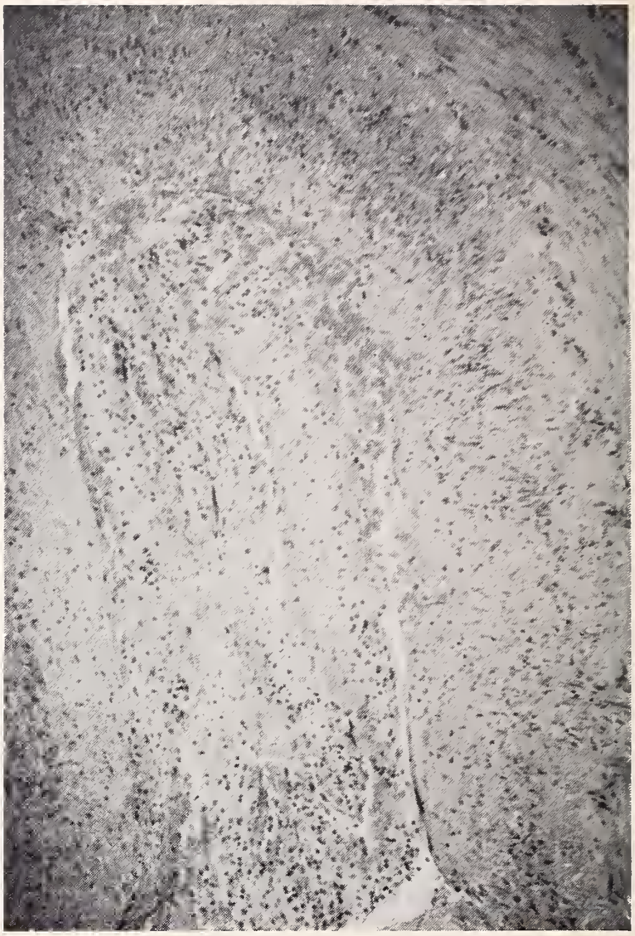

Figure 2.—Sagittal section. Partially organized and adherent thrombus in an inflamed temporal artery.

To date only one study of temporal arteries has been performed in a random group of autopsy examinations.[31] Progressive degenerative changes, reportedly indistiguishable from those of healed arteritis, were noted in temporal arteries of aged patients. All layers of the vessel wall were involved but giant cell changes were not present, except in two patients, in whom giant cell aortitis was likewise found.

One mechanism postulated for muscle pain and tenderness is that inflammation in arteries supplying the muscles may cause ischemia and pain withotu any histological changes. According to this postulation, involvement of subclavian arteries results in shoulder girdle pain and iliac artery involvement in pelvic girdle pain.

Electron microscopy was performed on the liver biopsy specimen in the one reported case in which results of liver function studies were abnormal.[28] Whereas light microscopy was normal, electron microscopy revealed changes in the ultrastructure of liver cells, mainly in the mitochondria and ergastoplasm. Also noted were abnormal glycogen distribution and abundant lipofuscin.

Differential Diagnosis

The early diagnosis of polymyalgia rheumatica may be difficult when only one group of muscles are affected. Gordon[21] discussed this matter in his excellent review article. Cervical spondylosis is common in the older age group which also suffers from polymyalgia, and the differential diagnosis of these two conditions may be very difficult indeed. Cervical osteoarthritis is suggested by x-ray studies showing narrowing of joint spaces and osteophytes, whereas a high ESR and, of course, tenderness of cranial arteries or a positive artery biopsy indicates polymyalgia. The presenting manifestations of multiple myeloma are back pain and accelerated ESR, but proteinuria, abnormal bone marrow showing increased plasma cells, a gamma spike on protein electrophoresis and x-ray changes of the spine are also expected. Nerve root pressure due to metastatic carcinoma of the vertebra or a lumbar disc prolapse will present with pain and, sometimes, increased sedimentation rate, but in such cases abnormalities are found on routine x-ray examination and myelography. Degenerative periarthritis of the shoulder is unilateral, constitutional symptoms are absent and the ESR is usually normal.

Systemic lupus erythematosus (SLE) and periarteritis nodosa may be considered in the differential diagnosis because of myalgias, arthalgias, constitutional symptoms and accelerated ESR. In SLE, the patients are younger, LE preparations or ANA are usually positive and many other symptoms are manifested. In periarteritis, one may find evidence of renal or pulmonary disease and necrotizing vasculitis. These patients are often quite ill and do poorly whatever the therapy. Polymyositis presents with muscle weakness and less frequently with pain and stiffness. In addition, there are often muscle atrophy, elevations of serum muscle enzymes (for example, SGOT, CPK, aldolase), electrocardiogram changes and abnormal muscle biopsy specimens. In carcinomatosis, systemic symptoms and accelerated ESR are present, but the response to therapy is poor.

Chronic brucellosis is characterized by arthralgias, malaise, low grade fever, sweating and muscle pains. However, the sweating is more pronounced and the pains are milder than in polymyalgia rheumatica, without especially affecting shoulders or hips. The diagnosis may be established by serologic testing or cultures. Rheumatoid arthritis in elderly people is similar to polymyalgia rheumatica. Frequently the ESR is accelerated, some of the patients have anemia, and shoulder involvement is present in more than half of them. However, other manifestations of joint disease, radiographic changes and abnormal serologic tests are also found. The presence of a positive latex fixation in an elderly person is quite common and, hence, may be misleading. Finally, psychoneurosis may be simulated because of vague pains and absence of objective findings. In this latter condition the ESR is normal.

Course

Even without treatment, polymyalgia rheumatica is usually self-limited, lasting from two to four years, with complete recovery.[21] Bagratuni,[16] however, found the mean duration of symptoms in his 50 patients to be seven years. It is possible that with the relationship between polymyalgia rheumatica and temporal arteritis becoming more apparent, severe sequelae such as blindness may be reported in association with the disease in the absence of appropriate steroid therapy.[15] Vascular thrombosis may also occur in other vital places.[32]

Complications

Perhaps temporal arteritis should not be listed as a "complication" of polymyalgia rheumatica, since each represents a segment of the same entity or similar manifestations of disseminated giant cell arteritis. Temporal arteritis occurs in at least one-third of patients with polymyalgia rheumatica.[13] Blindness is said to be a very common finding in temporal arteritis—it occurred in 73 of 175 patients reported by Hollenhorst[33] due to arteritis of the ophthalmic arteries. Forty to fifty percent of patients with temporal arteritis have visual involvement[34] and the loss of vision may be sudden and irreversible. Eye involvement has occurred in cranial or temporal arteritis even in cases in which temporal biopsy was negative.[35]

Classical temporal or cranial arteritis is manifested by severe head pains; by tenderness over the course of temporal and occipital arteries, which may be reddened, thickened and non-pulsatile; by failing vision; by myalgias, which usually precede the arteritis by weeks to years; and by undue carotid pressure sensitivity, scalp tenderness, fever and necrosis;[36] symmetrical peripheral neuropathy manifested by diminished sensation and weakness of several or all extremities and decreased deep tendon reflexes;[37] and ophthalmoplagia.[38] Examination of fundi may be negative or may reveal papillitis, exudates, perivasculitis with "sheathing" of vessels and optic atrophy. Laboratory findings include accelerated ESR, increased globulins and hypochromic anemia.

However, cranial arteritis may present in other than the classical way. Headache may be absent if the occipital arteries are not yet involved. Lingual arteritis produces recurrent ischemic episodes manifested by paroxysmal blanching of the tongue.[39] Other arteries may be involved with giant cell changes, including the aorta, internal and external carotids, iliacs, coronaries, occipitals and retinal vessels. These changes may produce, among others: aortic incompetence due to aortic arteritis; coronary artery disease; deafness and ear pain; and strokes. Elderly people are more subject to vasculitis involving the aorta and its main branches, especially the cranial vessels.[40]

Treatment

Corticosteroids produce prompt and dramatic relief of myalgic symptoms within days in virtually all cases. In addition, constitutional symptoms abate, ESR decreases and vascular complications (visual, cerebral, coronary, and others) are prevented. Gordon[21] followed eight patients without steroids and they remained symptomatic for periods of two to four years. He treated 13 patients with steroids and all responded. His regimen consisted of 30 to 40 mg of prednisone for 10 to 20 days, then tapering, and stopping the drug within five weeks. In some, a complete, sustained remission was accomplished with one course. When symptoms recurred, myalgias were less severe Several patients required repeated steroid courses and in one patient five courses were needed. Long courses were not used because of the danger of osteoporosis in the elderly.

Fessel and Pearson[15] advocated performing temporal artery biopsy and then treating all those persons who had positive biopsy with 40 to 60 mg of prednisone daily for 12 weeks. They expressed belief that most visual complications occur within 12 weeks of the onset of general symptoms of giant cell arteritis. A maintenance dose of 7.5 to 10 mg daily may be required for relief of pain over an extended period.

Wilske and Healey[14] use 30 mg of prednisone daily for one month in polymyalgia rheumatica. They then decrease by 5 mg every two weeks to a dose of 10 mg, and then by one mg every week, for a total course of approximately six months. They use salicylates and phenylbutazone as adjuncts while tapering steroids. Only 4 of 18 patients were able to discontinue steroids within six months, many requiring maintenance doses of more than 10 mg of prednisone for months.

When temporal arteritis was definitely present, steroids resulted in abatement of headache and myalgias and return of temporal artery pulsations.[41] Prompt use of steroids usually prevents sudden blindness, the incidence of blindness decreasing by 50 to 75 percent.[9] A patient with intermittent claudication was started on 40 mg of prednisone daily and after 13 months was still taking 10 to 15 mg daily. Claudication abated and there was arteriographic evidence of improvement of arterial narrowing. Once during the period when steroid dosage was reduced to below 10 mg daily, symptoms of claudication recurred.[22]

The use of salicylates has given unpredictable results in most patients. However Bagratuni found them to be efficacious.[16] Physical therapy may be helpful. Phenylbutazone and oxyphenbutazone are satisfactory in alleviating myalgia, although not as good as steroids. However, these two drugs are dangerous because they masked the development of temporal arteritis in four patients, in whom some visual loss resulted.[42]

Prognosis

The usual prognosis is favorable, with complete recovery the rule when steroids are instituted early. Total cessation of myalgias and other constitutional symptoms and relief of arteritic manifestations occur.

Illustrative Cases

Case 1. A 55-year-old woman had a history of progressive fatigue for one year and severe myalgias for six months. Myalgias began in the legs, knees and anterior thighs and more recently in the biceps, triceps, deltoids, groin, popliteal areas, medial thighs and in the posterior neck. She denied headaches, joint swelling or pain, but had noted morning gel and stiffness lasting approximately an hour. Diffuse tenderness and hypersensitivity of the scalp were present for six months and a tender area in one temporal artery had developed several weeks before examination. Medications she was taking included indomethacin, 25 mg four times a day, and aspirin, 30 to 40 grains daily.

Past history was unrevealing, except for an episode of left ophthalmoplegia ten years earlier, which improved over several months.

On examination, the left temporal artery was not prominent or readily palpable except just above the outer one-third of the left eyebrow where it was found as a tortuous, enlarged, slightly red, tender vessel. The optic discs and fundi appeared normal. All peripheral joints were normal. Muscular tenderness was elicited on compression of shoulder or pelvic girdle areas.

The ESR was 47 mm in one hour and both the latex fixation and ANA were borderline but not definitely positive. A left temporal artery biopsy showed intimal edema, pronounced narrowing of the lumen, elastic fragmentation in the media, adventitial inflammatory cell infiltrates and the presence of giant cell-like granulomata (Figures 1 and 2). Prednisone was instituted, 60 mg daily, with excellent response; the patient was essentially asymptomatic within 48 hours. Over the next several weeks the dosage was tapered to 15 mg daily, at which time minimal symptoms recurred and the ESR was 28 mm in one hour. On 20 mg of prednisone daily she remained essentially asymptomatic and the cranial arteries were no longer tender.

Case 2. A 75-year-old man was admitted with blindness of the left eye of four days duration. Three weeks earlier, aching pains had developed in the shoulders, neck, back and upper arms. These were associated with throbbing headaches that started at the vertex and radiated to the left eye and the left occiput. The patient also noticed an uncomfortable sensation on the left side of the head when brushing the hair or touching the scalp in that area. The various pains were rather mild and were readily relieved by 40 to 60 grains of acetylsalicylic acid per day. Two weeks after the onset of symptoms the patient was seen by a physician, who obtained laboratory studies with normal results except for an erythrocyte sedimentation rate of 35 mm in one hour (Wintrobe method). A week later the patient suddenly noted complete blindness of the left eye and was referred to the hospital. The headaches subsided spontaneously at about this time, but the other pains persisted.

There had never been previous symptoms of arthritis or related disorders. The family history was noncontributory.

Physical examination showed blurred disc margins bilaterally. A cerebral neoplasm was excluded by x-ray studies of the skull, electroencephalography, brain isotope scan and spinal-fluid examination.

During the first week in the hospital the patient had only slight, generalized aching discomfort. On the twelfth day vision in the right eye decreased. Visual loss was rapidly progressive during the next 48 hours. A biopsy of the left temporal artery was made, prednisone (60 mg daily) was started, and stellate-ganglion block was performed. After the institution of corticosteroid therapy the musculoskeletal symptoms subsided completely and the blindness did not progress, although vision did not improve. The temporal arteries, which had not been noticeably tender, did not appear to change in character. During the next nine months the patient continued to receive 40 mg of prednisone daily. The vision of the right eye did not further decline, but total blindness persisted in the left eye. The musculoskeletal symptoms in the neck, shoulders, arms and upper back have not returned.

Pertinent laboratory findings during the hospital course included normal hemoglobin and hematocrit and a creatinine of 1 mg per 100 ml. LE cells and antinuclear antibodies were absent, and the latex fixation test was negative. The sedimentation rate was 36 mm in one hour. The temporal artery biopsy showed acute and chronic inflammatory cells in all layers of a thickened blood vessel wall, with fibroblastic proliferation of the media, edema of the endothelial lining and thrombus formation. The features were consistent with temporal arteritis.

The first patient had myalgias and temporal artery tenderness without any ophthalmic manifestations, whereas in the second patient unilateral blindness developed shortly after the onset of myalgias. Possibly the vision in the other eye was preserved by prompt treatment with prednisone.

Conclusion

The current status of polymyalgia rheumatica remains somewhat unclear in the literature, because of differences in nomenclature and differing views regarding its relationship to cranial arteritis. It seems that the evidence linking these two conditions is overwhelming and that treatment for polymyalgia rheumatica should be aimed at preventing the sequelae of arteritis, whether or not biopsy evidence of arteritis is found. Since involvement of arteries may be patchy, a negative biopsy does not rule out the presence of arteritis. Polymyalgia rheumatica may be a form of arteritis in which cranial and other large arteries, and even the aorta, may be involved at various stages of the disease.[32]

The dosage and duration of steroid therapy will have to await further and longer follow-up studies. Meanwhile, it seems most appropriate to treat with moderately high doses of steroids, probably 30 to 60 mg of prednisone daily, for at least three months and then taper to 10 to 15 mg daily for a total of six months to a year, with discontinuance sooner if myalgias disappear. This proposal is made even though it is recognized that the present criteria for the diagnosis of polymyalgia rheumatica are incomplete. More studies on the incidence of arteritic changes in polymyalgia rheumatica are needed. Also, other causes for acceleration of ESR should be vigorously sought before steroid therapy is given to an elderly person. Finally, it would again be worthwhile examining temporal arteries in a large random group of elderly patients, at autopsy, to fully evaluate the changes that reportedly occur with aging.

Polymyalgia rheumatica may be more common than it has been thought to be. It should be thought of when an elderly person presents with pain in the neck and shoulders, especially in conjunction with an unusually accelerated ESR.[43]

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RECTOVAGINAL FISTULA FROM CANCER

"Once a patient [with pelvic cancer] has developed a rectovaginal fistula either from radiation alone or as a result of combination therapy, there will be very few fistulas, I think, that you can close sucessfully. In a majority of instances, you'll be wise to settle for a permanent colostomy. [One of my colleagues has] an elaborate procedure in which he developed a whole tag of omentum and tried to interpose that between the rectal defect and the vaginal wall; but I think there are few of us who are qualified to take on this procedure. I've done exenterations at times for extensive radiation damage, including those with the rectovaginal fistula; but for the most part I believe that the colostomy is indicated."

—Langdon Parsons, M.D., Boston

Extracted from *Audio-Digest Surgery,* Vol. 15, No. 22, in the Audio-Digest Foundation's subscription series of tape-recorded programs.

MEDICAL STAFF CONFERENCE

Diseases from Vietnam

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Associate Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. SMITH:* The Medical Grand Rounds this morning is being devoted to the medical fallout of our brisk foreign policy. The presentation of patients as well as the discussion will be given by Lieutenant Colonel John J. Deller. Dr. Deller we know as an old friend, since in addition to his army training he spent one year as a Fellow in Endocrinology and Metabolic Diseases here at the University of California. We are delighted to welcome him back and have him introduce both his topic and his patients.

DR. DELLER:† Thank you, Dr. Smith.

This morning I would like to review some of the medical problems seen in this country but which have originated in Southeast Asia. These problems have significance for physicians here in San Francisco; they are not remote tropical diseases found only in a textbook. Currently there are over 500,000 Americans in Vietnam. With the present rotation policy, these 500,000 Americans will return to the United States within a year, and with them will come tropical diseases.

Basically the medical community is faced with two problems: the recognition of diseases imported into this country for the sake of the "host patient" himself and, less immediate but more far-reaching, a significant public health problem in the introduction of new diseases into this country. I will deal mainly with the first of these considerations and only touch upon the potential of the latter.

It takes less than 20 hours to fly from Saigon to San Francisco. This brings the fighting-front fairly close. Thus, it is not at all unreasonable for us to expect any disease seen at a battalion clearing company or an evacuation hospital in Southeast Asia to appear at a community hospital in this country. Realization of this fact emphasizes the importance of tropical medicine in the United States, not only now but in the future. With increasing air traffic around the world, tropical diseases will be seen more and more in this country. Only by having a keen awareness of these diseases will we be able to make prompt, accurate diagnoses. Because some of these diseases are potentially fatal, early recognition may be critical.

In the limited time available, I shall concentrate on a small group of febrile illnesses which, because of their long incubation period, are likely to be seen in this country. Many of these patients will be seen by private physicians because most of the returning soldiers are either discharged from the service within a few days of arrival in the States or are given a 30-day leave.

It was from necessity that we became interested in tropical febrile diseases at the 93rd Evacuation Hospital in Vietnam. At first we had only the usual textbook knowledge of these diseases. It was very frustrating to admit large numbers of patients having a variety of indistinguishable febrile illnesses. We studied a number of these cases to establish some diagnostic criteria. When you read the chapters on tropical medicine in the standard textbooks of medicine, you find that all of the tropical febrile diseases seem to melt together and that there appear to be very few distinguishing features. In order to organize an approach to these illnesses, I have grouped them into five major disease categories (Table 1). The major arborvirus diseases seen in Southeast Asia are two in number: dengue, with which you are probably familiar, and chikungunya, which is esoteric by American standards. These in addition to scrub typhus, leptospirosis, and malaria constitute the biggest medical problems. Melioidosis is of significance because of its seriousness. (This list omits venereal disease, by far the commonest infectious disease among troops in Southeast Asia.)

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Table 2 is taken from our original study in which we attempted to define the various clinical manifestations of these febrile tropical illnesses. The diagnoses were proven by virological, bacteriological, or serologic tests.[1]

Dengue

Dengue is the most common arthropod-borne virus disease affecting our troops in Southeast Asia. A widely known disease, dengue was first recognized in the 1780s in Philadelphia—certainly no tropical climate. Since that epidemic the disease has cropped up from time to time throughout the country, mostly in army camps. The mosquitoes necessary for transmission of this disease do exist in the United States.

In Vietnam we were confronted with the problem of differentiating dengue from a number of more serious diseases. As will become apparent, fever, chills, and headache are characteristic of most of the tropical febrile diseases. However, it is important to know how high the fever goes and where the man was when he became ill, because, knowing these two simple facts, one can often distinguish between arborvirus diseases on the one hand and the "jungle-borne" diseases on the other. For example, patients with arborvirus infections rarely have temperatures above 104° F. This is an extremely important differential point because almost invariably a patient with malaria will have a fever rise above 104° F within the first 48 hours.

The arborvirus diseases, dengue and chikungunya, are transmitted primarily by the Aedes mosquito, an urban dweller. As a consequence, these diseases are not likely to be encountered in the jungle but are most frequently seen in an urban area or base encampment. Thus by asking the patient where he was within the 2 or 3 weeks preceding onset of symptoms, one can often predict whether the patient has an arborvirus disease or a "jungle-borne" disease such as malaria, leptospirosis or scrub typhus.

TABLE 1.—*Major Febrile Tropical Illnesses in Southeast Asia*

- Arborvirus Diseases
  - Dengue
  - Chikungunya
- Scrub Typhus
- Leptospirosis
- Malaria
- Melioidosis

The symptoms of dengue are not distinctive. Three-quarters of the patients have a "flu-like" illness with malaise, backache, anorexia, fever, and often severe frontal headache. They may present with lymph adenopathy, an important physical finding because patients with malaria do not have adenopathy and in patients with scrub typhus adenopathy develops only after several days of illness. A fleeting macular rash is present in at least one-third of the patients, and spontaneous petechiae occurring within this setting, especially on the lower extremities, are almost diagnostic for the arborvirus diseases. The tourniquet test may be positive in patients with dengue without an associated reduction in platelet count.

The course of dengue is variable. Generally fever and symptoms subside within 5 to 7 days, and few patients have a prolonged convalescence.

TABLE 2.—*Differential Features of Patients Having Dengue, Chikuugunya, Scrub Typhus, Leptospirosis, and Malaria*

	Dengue	*Chikungunya*	*Scrub Typhus*	*Leptospirosis*	*Malaria*
Epidemiology					
Camp, urban	†††	†††	—	—	—
Jungle	—	—	†††	†††	†††
Fever, F					
<104	†††	†††	†	†††	—
>104	—	—	††	—	†††
Arthralgias	—	†††	—	—	—
Tender adenopathy	†† (Early)	†††	††† (Later)	†	—
Tender liver or spleen	—	—	††	††	†††
Rash	†	††	††	—	—
Petechiae or positive tourniquet test	†	—	—	—	—
Leukocyte count per cu mm					
<5,000	††	††	—	—	—
>5,000	†	†	†††	†††	†††
SGOT >50 units	—	—	—	—	††

SGOT = serum glutamic-oxaloacetic transaminase; — = less than 25 percent; † = 25 to 49 percent; †† = 50 to 74 percent; ††† = 75 to 100 percent.

Adapted from Annals Inter. Med., 66:1129, 1967 and USARV Med. Bull., 2:23, 1967.

Chikungunya

The second arborvirus disease which may be acquired in Vietnam and transported back to this country is chikungunya. This disease was first recognized in Tanganyika in 1952 when an epidemic characterized by high fever and severe polyarthritis occurred among the natives. It was, however, self-limited. Fortunately, Dr. Ross[2] collected blood from many of the affected patients along with pools of Aedes mosquitoes, and in 1956 he isolated a new virus to which the name chikungunya was given—the natives' description, which means "that which bends up the joints."

Since the recognition of that original epidemic, chikungunya has been identified throughout Southeast Asia, southern parts of Africa, and India. It has had a wide spectrum of clinical features ranging from severe polyarthritis, which so far as I know has been self-limiting, to a dengue-like illness with mild arthritis, to hemorrhagic fever. The same virus has been cultured from all of these clinical varieties.

The one feature that distinguishes this disease from dengue is the arthritis. Even though dengue has been referred to as "break-bone fever," it is not associated with true arthritis. Severe myalgias and perhaps arthralgias may occur with dengue, but not arthritis. The polyarthritis of chikungunya is of great interest, for it represents an example of a known viral disease, from which an organism can be readily cultured, that can mimic both rheumatoid arthritis and acute rheumatic fever. It is very much like the epidemic polyarthralgia, which again mimics rheumatoid arthritis, reported in Australia and New Guinea. Chikungunya so closely resembles rheumatoid arthritis that our first three patients presenting with fusiform swelling of the proximal interphalangeal joints and bilateral synovitis of the wrists were initially diagnosed as having acute arthritis.[3] However, patients with chikungunya improve spontaneously and, although the arthritis may linger for several weeks, it does not develop into chronic arthritis. However, it is conceivable that if a viral disease similar to chikungunya had a strong antigenic potential, it could initiate an auto-immune reaction and lead to a chronic form of arthritis.

Except for the arthritis, chikungunya in American troops has been a mild dengue-like illness. It has not produced the severe crippling arthritis of the type reported in Tanganyika, nor has it caused hemorrhagic fever as occurs in dengue. It is a disease that should be considered in a Vietnam veteran who has an acute febrile illness.

It is important to recognize these two arborvirus diseases in order to distinguish them from diseases that are more important from the standpoint of morbidity and mortality.

Scrub Typhus

Scrub typhus is caused by a mite-borne rickettsia and presents with a typical triad of rash, eschar, and a positive therapeutic response to tetracycline. With these prominent features, it is usually easy to diagnose; unfortunately, not all cases behave this simply. Sometimes the eschars are hidden and may be overlooked on physical examination.

Like malaria, scrub typhus occurs in the jungle. The mites that carry the rickettsial organism breed in heavily forested areas of Vietnam; hence a history of a jungle environment is important. It has been said that these mites live and breed on the larvae of the Anopheles mosquito. I am not sure that this theory holds up, but at least the two diseases commonly occur together; indeed, malaria and scrub typhus may occur simultaneously in the same patient. The fever, chills, headache, malaise, adenopathy and backache common to all of these tropical diseases are also characteristic of scrub typhus. In addition, severe conjunctival injection, which we usually associate with leptospirosis, is common in scrub typhus. The most important features are a macular rash, which is usually not as fleeting as the rashes of the arborvirus diseases, and an eschar. The eschar typically resembles a cigarette burn. It is not surrounded by significant inflammatory reaction and usually has a black necrotic center with a narrow rim of erythema. There is no associated lymph angitis or lymph adenitis. This lesion is important to recognize because in melioidosis, which I will discuss later, a skin inoculum can present in a similar manner, except that there is a much greater reaction and associated lymph angitis.

It is important to treat suspected scrub typhus with tetracycline. Of the tropical diseases, only scrub typhus responds dramatically to tetracycline therapy (1 gram every hour for four doses followed by 1 gram every 6 hours for 7 days). Within 48 hours, and often within 12 hours, there is a dramatic drop in fever. It is important to treat scrub typhus early, for if the disease goes untreated for 2 weeks, there is an alarming morbidity. Most of our patients in whom the disease was not recognized for 2 weeks had to be evacuated to the United States and were ill for 6 to 8 weeks.

Leptospirosis

In leptospirosis the patient is not bitten, but has only to come in contact with leptospires breeding in the mud banks and rice paddies. Leptospirosis closely mimics dengue and scrub typhus and has very few distinguishing characteristics. It has been called "pseudodengue." It most closely mimics scrub typhus because of the generally high, spiking fevers. Conjunctival suffusion is an important sign, but it does not distinguish leptospirosis from scrub typhus. Gastrointestinal complaints and hepatic tenderness are common, which makes for confusion of this disease with malaria. A laboratory finding of leukocytosis is occasionally helpful, since most of the other tropical diseases are characterized by a normal leukocyte count or by leukopenia.

Leptospirosis actually encompasses an entire spectrum of diseases from a benign, self-limited form such as our troops are experiencing to a severe, hemorrhagic disease with severe jaundice and renal failure. Since our troops fortunately have acquired the benign form, there have been no serious complications. The benign form of leptospirosis is self-limited and requires no specific therapy.

Malaria

Malaria is the tropical disease which is of most concern to military physicians because it accounts for the largest number of patients. The malaria seen in Vietnam may be quite different from that seen in San Francisco. About 98 percent of the cases of malaria diagnosed in Vietnam result from *Plasmodium falciparum,* whereas 80 percent of the cases seen in this country result from *Plasmodium vivax.* The reason for this difference is the chloroquine-primaquine chemoprophylaxis or "suppressive therapy" program that is being used in Vietnam. Usually once a soldier leaves the endemic area, he neglects to take the drugs, even though he is given an 8-week supply, and with discontinuance of therapy the disease becomes manifest. Of 29 consecutive patients with vivax malaria admitted to Letterman General Hospital within the past year, not one had taken the medication after getting off the airplane! Subsequently a larger group of patients who did not have malaria after returning to this country were surveyed, and 60 percent of them had not taken the chemoprophylaxis after leaving Vietnam.[4]

The reason so much falciparum malaria is seen in Vietnam is that the current drug therapy is not suppressive for *Plasmodium falciparum.* In the last year there have been more than 2,000 cases of malaria diagnosed in American soldiers in this country. This figure could probably be expanded many times by including in it those patients who have left the service and therefore are not reported to the Surgeon General.

Malaria is generally easy to diagnose. All one needs is a high index of suspicion, a blood smear, and a technician or physician who knows how to interpret the smear. The majority of patients with malaria will have fever above 104° F within the first 72 hours of illness; frequently the temperature goes to 105° or 106° F. The differentiating feature is that such elevations are extremely rare with the other tropical diseases. Of course the shaking chill, a hallmark of malaria, is generally present, accompanied by headache and a variety of gastrointestinal complaints in over three-quarters of the patients. The most remarkable feature about the physical examination is the absence of specific findings. Except for percussion tenderness over the liver or spleen, or both, the examination is usually negative unless the patient has one of the major complications. Notably absent are the "typical" fever patterns and splenomegaly found in textbook descriptions of malaria. This absence is attributable mainly to prompt diagnosis and early treatment.

For the diagnosis of malaria, a high index of suspicion is critical. Once malaria is considered, a series of blood smears, both thick and thin, should be done to confirm the diagnosis. If you're lucky, on a thin smear you will see typical ring forms. Frequently, however, the thin smear will not reveal ring forms within the erythrocyte, and a thick smear will be necessary. The parasites may be fragmented and difficult to diagnose. In falciparum malaria the ring forms are only about one-fifth as large as the vivax forms. The gametocytes of falciparum malaria, however, are quite typical and easily recognized. Unlike the diseases previously discussed, which manifest themselves within 3 weeks, malaria may have a long latent period. Most of the vivax malaria in this country is diagnosed in patients who have left an endemic area more than 50 days before; therefore, this disease is very likely to be seen by private physicians.

The treatment of malaria has undergone several changes since the appearance of resistance strains of *Plasmodium falciparum* in Vietnam. Currently, however, the proper treatment can effect a cure in probably 98 percent of cases. In my personal experience with more than 1,200 patients at one hospital, 20 of whom had cerebral complications and three of whom had renal failure, there were no fatalities. Standard treatment for vivax malaria has not changed, as *Plasmodium vivax* has not demonstrated any resistance to chloroquine and primaquine. *Plasmodium vivax* continues to go through reproductive cycles within the reticuloendothelial system; therefore, primaquine is given for at least 14 days in an attempt to eradicate the parasites in this "exoerythrocytic phase."

The treatment schedule for *Plasmodium vivax* infection is as follows: chloroquine phosphate, 1.0 gram (600 mg base) immediately, followed by 0.5 gram in 6 hours and 0.5 gram daily for 2 days. Primaquine, 15 mg base, is given daily for 14 days.

Since as high as 50 percent of *Plasmodium falciparum* infections acquired in Vietnam have been relatively resistant to chloroquine, patients with this infection must be treated with quinine. Quinine, when used properly, is a relatively safe drug. When it is used alone, there is perhaps a 5 to 10 percent failure rate; however, the addition of pyrimethamine (Daraprim®) and possibly a sulfone (Dapsone®) or sulfa drug will approach a 100 percent cure rate for initially treated *Plasmodium falciparum*. Currently, triple therapy for falciparum malaria is recommended. The treatment schedule is as follows: quinine, 650 mg every 8 hours for 10 to 14 days, followed by pyrimethamine, 25 mg, every 12 hours for 2 to 3 days and Dapsone®, 25 mg, given daily for 28 days. Many patients who were treated for *Plasmodium falciparum* in the past have had "recurrences" with *Plasmodium vivax* simply because they did not receive any primaquine.

Table 2 reviews the major points in differential diagnosis of the disease most likely to mimic malaria in a person returning from Vietnam. Where the infection was acquired and how high the temperature rose may be the two most important clues as to whether one is dealing with a treatable infection (malaria or scrub typhus) or a self-limited one.

Melioidosis

Melioidosis may be relatively new to most of you. It was originally recognized in Rangoon in 1912 by Whitmore and Krishnashwami, who reported on a number of street beggars dying with what appeared to be distemper because of the tremendous frothy sputum produced before death. A glanders-like microorganism was subsequently isolated and given the name *Malleomyces pseudomallei.* This disease was next recognized about 5 years later in ante mortem studies by Fletcher and Staunton in Malaya in 1917. Melioidosis has subsequently been found in a variety of forms, most simply classified as follows:

- Acute—pneumonic and septicemic
- Chronic—pulmonary and systemic
- Subclinical—serologic evidence only

The acute form can present as overwhelming pneumonia or as septicemic illness which usually terminates as pneumonia. The chronic variety can masquerade as tuberculosis. This is the type with which I think we should concern ourselves because this is the type that may well be seen here in San Francisco. The chronic variety may also present with manifestations such as chronic draining abscesses or osteomyelitis. It has also been shown that there is an "iceberg effect" in this disease, in that there have been a large number of cases with only serologic evidence of past exposure to this infection. In one Thailand study, approximately 8 percent of the population tested had serologic evidence of previous contact with this organism. Although we are not seeing a large number of cases of melioidosis, there have been more than 60 cases reported since May 1966, in Americans in Vietnam or recently returned from there. It is an important disease because it may be lethal in the acute form and also because of the possibility of transplantation into this country. The organism is ubiquitous.

A keen awareness of the clinical spectrum of melioidosis is the key to diagnosis. A chest roentgenogram will often provide the immediate clue. The organism *Pseudomonas pseudomallei* will grow readily on blood agar media; in fact, sometimes it grows so readily that it is thought to be a contaminant. A smear from the culture, stained with either Gram's or Wayson's stain, provides a clear-cut diagnosis in most cases. The organism appears as small pleomorphic, Gram-negative, bipolar rods that resemble small safety pins. Further identification can be made by sugar fermentation studies or specific serologic tests.

I would like to review briefly the major ways in which this disease may present. In our febrile disease study, we encountered two cases of the septicemic illness which presented with a cutaneous ulcer (presumably the site of entry of the organism), spiking fever, tremendous cellulitis and lymph angitis, and eventually meningitis and pneumonia. The two patients died without diagnosis having been made. Although they were treated with a large number of antibiotics, there was no obvious effect on the illness. This disease in its septicemic form is almost uniformly fatal when unrecognized.

The clinical course of the acute pneumonic variety varies from death within hours to death within days. It is an overwhelming infection; in fact, it is the most rapidly progressive pneumonia that one is likely to encounter. We saw one patient who had acquired this disease, so far as we know, within 5 hours of his death. In this rapidly progressive form, the disease is probably untreatable and is very much like plague pneumonia.

The form of disease which we are now seeing in this country is the chronic, more benign pulmonary infection which often presents with cough, low-grade fever and a roentgenographic appearance which immediately conveys the impression of tuberculosis. A negative tuberculin test and a history of travel to an endemic area should alert one to this disease.

The treatment of *Pseudomonas pseudomallei* infection will vary with the clinical type of disease. When we were first confronted with the acute varieties in Vietnam, we used standard antibiotic schedules, including novobiocin and chloramphenicol. Despite such therapy our first five patients died. We found on serum inhibition studies that even in the undiluted serum there was no inhibition of growth of the *Pseudomonas pseudomallei* with the antibiotic schedules used. We eventually found that a combination of massive doses of chloramphenicol, novobiocin and kanamycin was necessary to arrest the overwhelming infection. Doses as high as 12 grams of chloramphenicol, 3 grams of kanamycin and 6 grams of novobiocin are necessary. With such treatment the next five patients survived. Such heroic therapy, however, has not been necessary with the more chronic variety of disease. It can be treated with as little as 1.0 gram of tetracycline daily. Naturally, sensitivity studies are required in every case.[5]

In summary, it should be emphasized that one must maintain a high index of suspicion of melioidosis in a patient who has been in an endemic area. This disease may lie dormant for years. In the French experience in the 1940s the disease was cropping up in France as late as 3 years after the return of troops from Southeast Asia.

QUESTION: What is the policy concerning blood transfusions from Vietnam returnees?

DR. DELLER: I believe the current policy is that no one who has been in an area endemic for malaria should be a blood donor for a minimum of 2 years, and this may be revised to exclude such potential donors indefinitely.

DR. SCHMID:* In cases of leptospirosis, do you have any meningeal manifestations?

DR. DELLER: Yes, meningeal manifestations are seen; in fact, the patients frequently will have what is thought to be meningismus. The same manifestations will be seen in scrub typhus. We followed several patients clinically and found that the lymphadenopathy which developed in the cervical areas after several days is probably what was initially mistaken as meningismus. In a few cases we performed spinal taps, and the taps were negative. I think the tender cervical adenopathy often will be masquerading as meningismus.

QUESTION: Have you witnessed any outbreaks of plague?

DR. DELLER: So far as I know we have had only three cases of plague in American servicemen. As you know, plague immunizations have been quite effective. The current plague immunization program, apparently, is keeping the incidence of plague in the American soldier quite low. Certainly plague is very high in the Saigon area and throughout Southeast Asia. We see large numbers of cases in the population there. I am just hopeful that we will be able to continue with our luck in keeping this disease suppressed in the American population.

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*Rudi Schmid, M.D., Professor of Medicine.

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Interdepartmental Conference

FROM THE UNIVERSITY OF CALIFORNIA, LOS ANGELES, SCHOOL OF MEDICINE

Systemic Lupus Erythematosus

MODERATOR: EUGENE V. BARNETT, M.D.
DISCUSSANTS: GARY KANTOR, M.D., YALE B. BICKEL, M.D.,
RUNE FORSÉN, M.D., AND HARVEY C. GONICK, M.D.

■ *Systemic lupus erythematosus is a polysystemic disease with a high incidence of associated glomerulonephritis. Patients with* SLE *rarely have the destructive arthritis so characteristic of rheumatoid arthritis. An unusual case is presented in which both glomerulonephritis and destructive arthritis occurred simultaneously, justifying the diagnosis of both systemic lupus erythematosus and rheumatoid arthritis.*

Immunohistochemical studies in lupus glomerulonephritis suggest that the pathogenetic mechanisms involve the deposition of immune complexes containing "nuclear" antigens and antinuclear antibodies in the lesions. The detection of mixed cryoglobulins in the sera of patients with SLE *suggests that a portion of the circulating immune complexes may precipitate at reduced temperatures and be detected as mixed cryoglobulins. The therapy of lupus glomerulonephritis with combinations of corticosteroids and azathioprine, though still in an investigative state, holds great promise. Similar abnormalities in diseases of minks and mice and in* SLE *suggest similar pathogenetic mechanisms in the three species involved. Since the diseases in the lower animals have been associated with persistent viral infection, the investigation of the role of persistent infection in* SLE *seems warranted.*

DR. EUGENE V. BARNETT (Department of Medicine)*: Our task is to report a multifaceted approach to the understanding of systemic lupus erythematosus. I think that, perhaps, when we have completed our discussions, we may decide that the term *systemic lupus erythematosus* is not the name of a disease but rather the title for a series of questions. Dr. Gary Kantor will start by discussing the simultaneous occurrence of systemic lupus erythematosus and rheumatoid arthritis.

Differentiation of Systemic Lupus Erythematosus and Rheumatoid Arthritis

DR. GARY KANTOR (Department of Medicine and Wadsworth Veterans Administration Hospital): The case presented is that of a 46-year-old white, married housewife who was initially seen in the medical clinic five years ago for evaluation of polyarthritis. She was in good health until 1958, when swelling and stiffness developed in the metacarpal-phalangeal (MCP) joints of her hands.

Oral corticosteroid preparations were administered from 1958 to 1961 and then replaced with salicylates. She continued to note intermittent joint swelling and morning stiffness. From 1961 to 1963 progressive deformity developed in her hands and feet, with additional involvement of the shoulders, hips and knees. On evaluation in the medical outpatient department in 1963, examination revealed subluxation and ulnar deviation at the MCP joints, swelling of the proximal interphalangeal (PIP) joints of both hands, synovial proliferation and effusion in both knees, additional deformities in the metatarsal phalangeal joints, and subcutaneous nodules.

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*Some patients reported in this study were in hospital at the Clinical Research Center of UCLA, CRC Grant No. RR00238.

Reprint requests to: Department of Medicine, University of California, Los Angeles, School of Medicine, Center for the Health Sciences, Los Angeles, Ca. 90024 (Dr. Barnett).

Laboratory data included a normochromic, normocytic anemia, normal urinalysis without proteinuria or sedimentary abnormalities, latex fixation titer of 1:5120, negative lupus erythematosus (LE) cell preparations, and creatinine content of 0.6 mg per 100 ml. Radiographic studies confirmed the presence of articular erosions involving the wrists, MCP and PIP joints, as well as subluxations at the MCP joints.

In March 1964, synovectomy of the MCP joints of the right hand was carried out. Pathological diagnoses included chronic active rheumatoid synovitis and chronic osteitis. Microscopic hematuria was noted for the first time on this occasion.

In February 1965, an erythematous malar rash, aggravated by exposure to sunlight, developed. Biopsy of a specimen of skin was consistent with LE, revealing small vessel vasculitis. Topical steroids were effective, although exacerbations continued after exposure to sunlight.

In August 1965, urinalysis revealed 2+ proteinuria and a quarter field of red blood cells. The LE cell preparation was positive, and antinuclear antibody (ANA) titer was greater than 1:256. Raynaud's phenomenon developed.

In March 1966, the ANA and latex fixation titers were unchanged, and the LE cell preparation was again positive. A 24-hour specimen of urine contained 4.9 grams of protein. The presence of a subcutaneous rheumatoid nodule was confirmed histologically. A percutaneous biopsy revealed glomerulonephritis consistent with systemic lupus erythematosus, and focal glomerular basement membrane deposits of IgG and beta $_1$c-globulin were demonstrated with immunofluorescent microscopy.[15]

During a five-month course of prednisone, 45 mg per day, creatinine clearance fell from 140 to 69 ml per minute, and serum complement remained low. In October 1966, azathioprine in a maintenance dose of 200 mg per day was added to the prednisone.

Chart 1 summarizes the patient's course during the first 12 months of azathioprine therapy. The creatinine clearance stabilized, and the serum gamma globulin (IgG) concentration and ANA titer decreased. At present she is taking 100 mg of azathioprine and alternating doses of 10 and 7.5 mg of prednisone per day.

Recent studies showed a creatinine clearance of 85 ml per minute and 24-hour urinary protein of 0.5 grams. A serum complement was 47 C'H50; ANA, positive in undiluted serum only; latex fixation titer, 1:40,980. A repeat renal biopsy 13 months after the institution of azathioprine revealed mild chronic glomerulonephritis with less activity of the glomerular process than noted previously. Focal IgG and beta $_1$c-globulin deposits persisted. The patient has done quite well since the orthopedic procedure. Although she has residual deformities, her functional impairment is relatively mild. There has been no recurrence of the transient hypertension present when she first had some evidence of kidney disease. The rash on her face gives difficulty only upon exposure to sunlight.

This patient's case has several quite unusual features that provide an opportunity to discuss the relationship between rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Before the advent of the LE cell preparation in 1948,[35] the diagnosis of SLE was extremely difficult to make. Pathological criteria were important but often unavailable to the clinician. Currently there are several pathological findings which may be helpful.

The presence of hematoxylin bodies has been considered pathognomonic of SLE.[37] They appear as small lilac-staining bodies in localized areas of necrosis including the glomerulus, lymph nodes, spleen and endocardium. Phagocytosis of this material by neutrophils is rarely noted *in vivo*. These bodies are not frequently present in the relatively small amount of tissue provided by percutaneous renal biopsy. The wire loop lesion seen within the glomerulus is suggestive of SLE, but nevertheless nonspecific.[16] Periarterial lamellar fibrosis or "onion-skinning" is frequently seen in the spleen,[48] but may on rare occasions be seen in other processes.[41] Libman-Sacks endocarditis has also been considered specific for SLE.[33] Adequate evaluation of the majority of these tissues

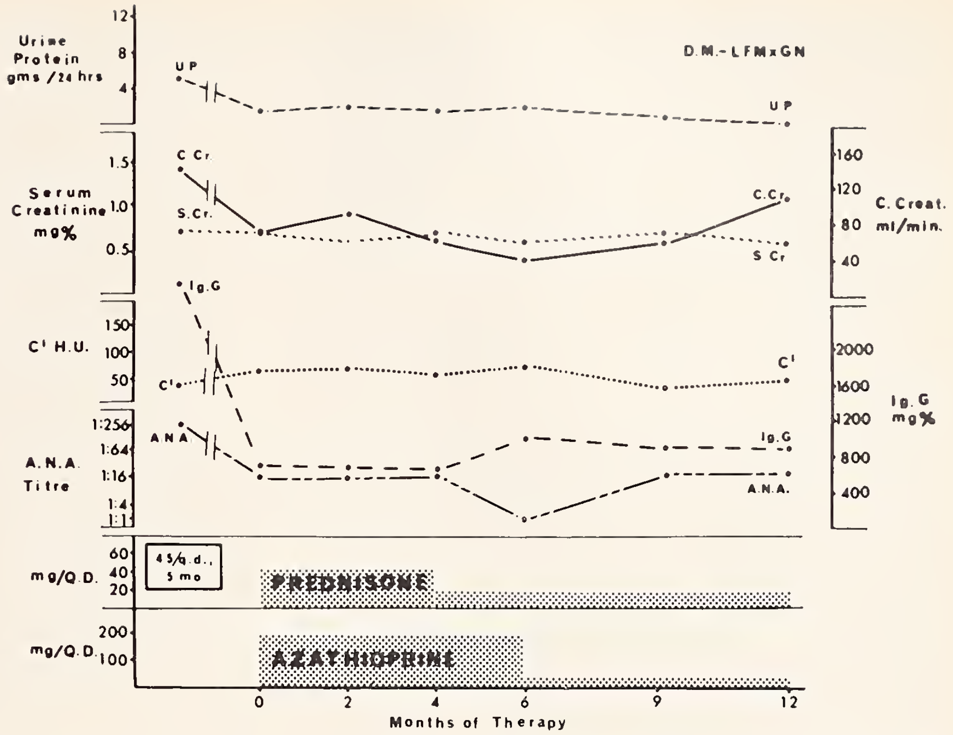

Chart 1. — Summary of patient's course outlining serial determinations of serum creatinine, complement, antinuclear antibody titer, and IgG concentration; creatinine clearance and 24-hour urinary protein. (Courtesy of Dr. James Drinkard.)

remains unavailable to the clinician, and as a result other means must be used in establishing the diagnosis.

Specific criteria for the diagnosis of SLE are not currently in widespread use. In general, however, the presence of multisystem disease, often including glomerulonephritis, in addition to the presence of LE cells or antinuclear antibodies is sufficient to make the diagnosis of SLE. When very sensitive tests are used to detect the presence of ANA,[39] a negative test in a patient who is not receiving steroid or immunosuppressive therapy but has active disease excludes the diagnosis of SLE.

A variety of other conditions for which specific or curative therapy is available must be excluded. A young secretary with known discoid LE was admitted to our hospital with fever and acute inflammatory arthritis involving a knee and ankle. The relationship of this episode to her menstrual period suggested a diagnosis of gonococcemia and gonococcal arthritis. She responded to intravenous penicillin, and subsequent blood and cervical cultures confirmed this diagnosis. Although ultimately other evidence suggestive of SLE developed, the utilization of salicylates or even steroids during this episode in lieu of specific antibiotic therapy might have resulted in serious complications.

Subacute bacterial endocarditis with fever, pleuritic pain, central nervous system involvement, arthritis, and focal glomerulonephritis provides another example. The renal lesion may progress to azotemia or uremia, at which time fever may be minimal or absent, and the diagnosis more difficult to establish. In this situation a negative ANA test excludes the diagnosis of SLE.

In addition, we have seen a young female with well documented multisystem disease clinically consistent with SLE in whom LE cell preparations and ANA titers were negative over a period of several years. Ultimately accelerated hypertension and azotemia developed and she died with uremia. Postmortem examination revealed systemic sclerosis without scleroderma, that is, without cutaneous involvement. During her illness the diagnosis of seronegative SLE had been considered.

The patient whose case was presented at the beginning of this discussion fulfilled the American Rheumatism Association (ARA) criteria[69] of classic RA, and subsequently evidence diagnostic of SLE developed. In order to evaluate the relationship between these two disorders, charts of patients with either RA or SLE who have been seen at UCLA within the last two years were reviewed. For purposes of comparison, the ARA criteria for the diagnosis of RA were employed, though ignoring the exclusion clause relating to the presence of LE cells. Similarly, a composite of clinical and laboratory criteria was utilized for the diagnosis of SLE. The presence or absence of seven features was noted, including characteristic malar rash, fever, serositis, non-erosive arthritis, small vessel vasculitis, glomerulitis or glomerulonephritis, and signs or symptoms of central nervous system involvement. The presence of radiographic erosions was not considered an exclusion. The results of LE cell preparations and ANA determinations were noted. The diagnosis of *possible* SLE was utilized in the presence of one clinical criterion and a positive result in one of the above laboratory tests, *probable* SLE with two clinical criteria and one laboratory test, and *classic* SLE with three clinical criteria as well as a positive LE cell preparation. The incidence and titer of rheumatoid factor[12] was also determined in both groups. These data, not including the patient presented, are summarized in Table 1.

Charts of 32 patients with RA were reviewed, including 15 with criteria of classic RA, 14 with definite RA, and three with probable RA. Tests for ANA were positive in 3 of 32 and for rheumatoid factor in 27 of 32 patients studied. Radiographic findings consistent with RA were noted in 22 of 24 patients and included 12 with definite articular erosions. Clinical, laboratory, or pathological evidence of glomerulonephritis was not noted in any patient with RA.

Charts of 47 patients with SLE were similarly reviewed, including 21 with criteria of classical SLE, 23 with probable SLE, and three with possible SLE. Tests for ANA were positive in 44 of 45 patients and for rheumatoid factor in 14 of 47 patients studied. Radiographic studies of the joints were obtained in 14 cases and revealed evidence of subluxation in one patient. However, erosions were not noted in any patient. Nephritis was present in 28 patients.

These data are consistent with a review of the literature since the introduction of the LE cell preparation 20 years ago. Although joint deformity and radiographic changes suggestive of RA have been previously noted in patients in whom the diagnosis of SLE has been considered, documented erosive arthritis is very rare.

Relevant to this observation, the renal service at Wadsworth Hospital saw recently a 74-year-old white man in whom the diagnosis of SLE was made in 1951 after arthritis, fever and chest pain developed and an LE cell preparation was positive. Joint deformity developed during the next seven years and resulted in MCP ulnar deviation and subluxation. At present, 17 years after the onset of joint symptoms, pronounced deformities persist. Nevertheless, current x-ray films still do not reveal articular erosions, although subluxation at the MCP joint is noted (Figure 1). A positive LE cell preparation at the onset of illness and the current lack of articular erosions would be most unusual in a patient with RA.

TABLE 1.—*Summary of Data in 32 Rheumatoid Arthritis* (RA) *and 47 Systemic Lupus Erythematosus* (SLE) *Patients*

Disorder	*Rheumatoid Factor*	*Antinuclear Antibodies*	*Radiographic Erosions*	*Glomerulonephritis*
RA	in 27 of 32	in 3 of 32	in 12 of 24	in 0 of 32
SLE	in 14 of 47	in 44 of 45	in 0 of 14	in 28 of 47

In another patient with classic SLE and joint deformity but no radiographic evidence of erosions, synovectomy revealed findings consistent with degenerative arthritis with articular fibrosis. Typical granulation pannus was not present. Other reports indicate that there may be minimal or absent histological changes in the synovium associated with the articular complaints in SLE in contrast to RA.[48] The absence of pronounced synovial hyperplasia and associated increased intra-articular pressure in SLE may account for the absence of erosions.

Results of numerous studies utilizing percutaneous renal biopsy or postmortem material on consecutive patients indicate that glomerulonephritis does not occur as part of RA.[31] Renal abnormalities in RA include amyloidosis, interstitial nephritis, papillary necrosis associated with analgesic abuse, and arteriolo or arteriolar nephrosclerosis.[49]

The rarity with which glomerulonephritis occurs in RA has led to the hypothesis that rheumatoid factor in some way alters antigen-antibody complexes, and thereby protects against the development of nephritis.[17] Data from this series does not confirm this concept. Significant titers of rheumatoid factor were noted in 14 SLE patients, six of whom had lupus nephritis, including one patient with a latex fixation titer of 1:40,980.

A prime diagnostic consideration relates to the presence or absence of nephritis in patients with SLE. Without nephritis the manifestations of the disease may frequently be managed with salicylates or low-dose corticosteroid preparations. In the presence of renal disease, high-dose steroid or immunosuppressive therapy is considered.[20] Although sometimes difficult to distinguish from SLE clinically, RA in association with either diffuse vasculitis, amyloidosis, progressive renal impairment, or positive LE cells, is nevertheless not SLE.

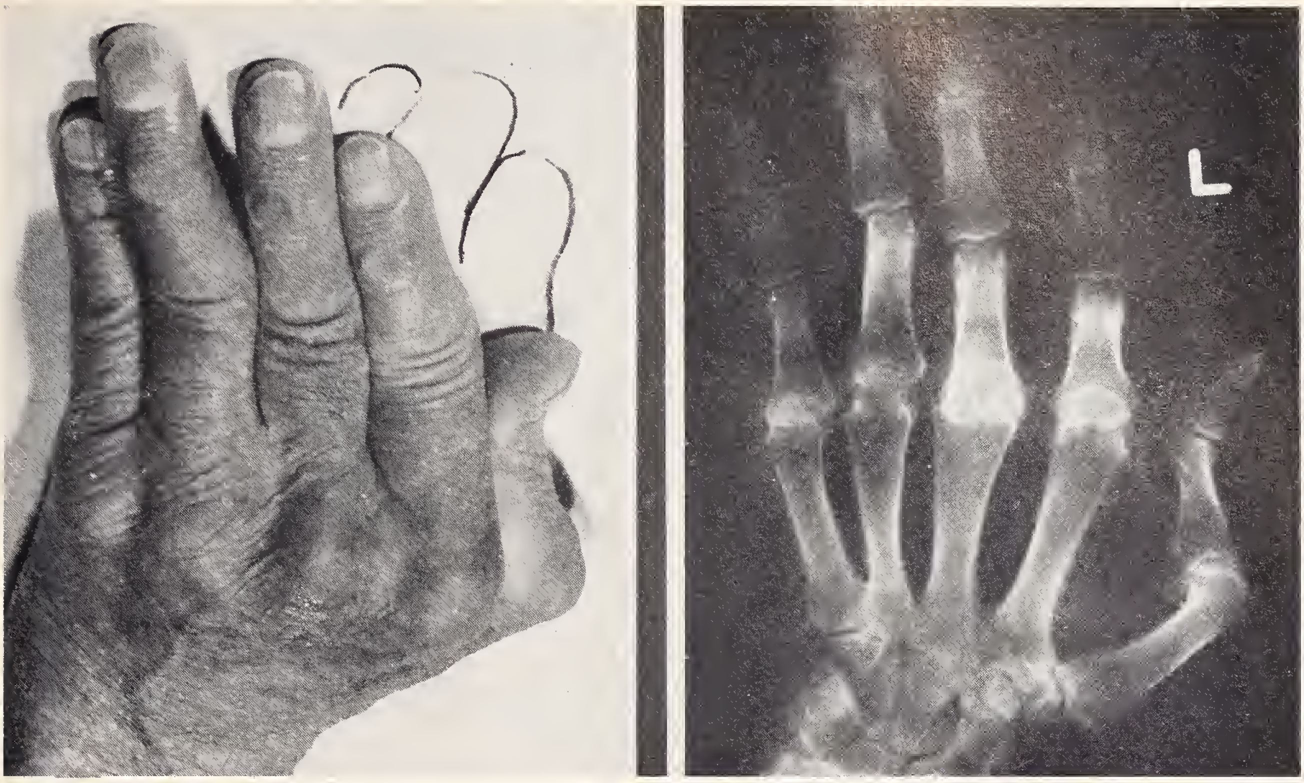

Figure 1.—*Left:* Chalk outline of the fingers, drawn with ulnar deviation passively reduced and both hands pressed firmly on the table to prevent ulnar deviation. *Right:* Radiograph of same hand, revealing subluxation at the metacarpal-phalangeal joint without articular erosions.

In this situation, articular erosions usually provide convincing evidence for the diagnosis of RA.

In summary, the diagnosis of SLE is based upon the existence of certain clinical features associated with the presence of LE cells or ANA. Other conditions, particularly when specific or curative therapy may be available, must be excluded. Except while receiving corticosteroid or immunosuppressive therapy, the absence of antinuclear antibodies in the presence of active disease excludes the diagnosis of SLE. Pathological features may be helpful, but are not sufficiently available to the clinician. The coexistence of RA with SLE, SLE with erosive arthritis, and RA with glomerulonephritis are all extremely rare. The presence of rheumatoid factor does not protect against the development of glomerulonephritis.

Nuclear Antigens and Antinuclear Antibodies in Lupus Nephritis*

Dr. Yale B. Bickel (Department of Medicine and Harbor General Hospital): Considerable evidence has accrued implying that lupus nephritis and other diffuse glomerular diseases arise as a consequence of immunologic mechanisms.[58] Similarities between these disorders and experimentally induced immunologic renal diseases suggest that there are two distinct pathways by which nephritis may develop. In nephrotoxic serum nephritis,[53] antiglomerular basement membrane (anti-GBM) antibodies invoke renal injury by combining with antigenic sites on or within the glomerular basement membrane, consuming complement in the reaction. Immunofluorescent studies performed on renal tissue from involved kidneys revealed the presence of linear deposits of immunoglobulins and complement components (beta $_{1}$C-globulin) along the basement membrane.[63] A similar pattern of immunoglobulin deposition may be found in the kidneys of patients with Goodpasture's syndrome[24] and chronic progressive glomerulonephritis.

Experimental nephritis may also be produced by the intraglomerular deposition of antigen-antibody complexes.[19] In these instances, immunofluorescent studies reveal the presence of granular or "lumpy-bumpy" deposits of immunoglobulin and complement,[18] corresponding to electron-dense subepithelial deposits within the basement membrane visible by electron microscopy. Morphologically similar findings occur in lupus nephritis[27,46,65] and in post-streptococcal glomerulonephritis,[1,57] suggesting that in these diseases the kidney is injured as an "innocent bystander" by the deposition of antigen-antibody complexes arising in the circulation.

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*This project was supported in part by a grant from the Southern California Arthritis Foundation.

Antinuclear antibodies reactive with a variety of nuclear antigens may be detected in the sera of virtually all patients with active, untreated SLE.[6] Although these antibodies exert no direct cytopathic effect when transfused into normal recipients,[52] on transplacental transfer,[11] or when introduced into tissue cultures,[80] they may participate in immunologic injury by combining with nuclear antigens to form circulating phlogistic complexes capable of depositing within the kidneys. The granular pattern of deposition of immunoglobulins and complement within the basement membrane[65] and the consistently decreased serum complement level during active stages of nephritis[25,47,60,79] support this concept. Additional observations in SLE lend further credence to the role of nuclear antigen-ANA complexes in invoking renal injury. It has been shown that the ratio of light chain types within immune deposits in SLE is independent of their serum ratio[38] and there is, in general, a correspondence of the classes of bound immunoglobulins to serum titers of each antinuclear immunoglobulin.[75] These data suggest that glomerular-bound immunoglobulins represent specific antibody globulin deposits rather than immunoglobulins "trapped" from the circulation independent of antibody activity.

ANA's reactive with DNA, nucleoprotein, and phosphate buffer-extractable nuclear antigens have been eluted from isolated glomeruli of lupus kidneys.[28,32,44,45] *In vivo* localization of ANA to nonviable renal nuclei paralleling the immunopathology of the cutaneous lesions of SLE[77] cannot account for the presence of these antibodies in eluates from affected kidneys, since such *in vivo* reactions occur only rarely in the kidney.[65] *In vitro* reaction of serum ANA with nuclear antigens liberated during the isolation of glomeruli likewise does not explain the presence of ANA in such eluates, since quantitative determinations demonstrate higher antibody concentrations expressed in activity per unit of gamma globulin in the eluates compared with corresponding sera.[44] Other antibodies found in the sera are absent in the eluates, further supporting the belief that there is deposition and concentration of ANA-containing complexes within the glomerular basement membrane.

TABLE 2.—*Evidence in Support of the Role of Nuclear Antigen-Antinuclear Antibody Complexes in the Pathogenesis of Nephritis in* SLE

1. Immunoglobulins and complement are present in granular immunofluorescent and electron-dense deposits within the basement membrane of affected glomeruli[65] similar to the findings in serum sickness.[19]
2. Acid buffer and molar saline eluates which dissociate antigen-antibody complexes contain antinuclear antibodies in concentrations greater than in corresponding sera.[28,32,44,45]
3. Eluates from deoxyribonuclease-treated isolated glomeruli contain antinuclear antibodies specific for DNA and nucleoprotein.[44]
4. Serum complement levels are depressed during periods of active nephritis.[25,47,60,79]
5. DNA antigen has been demonstrated in the serum of some patients with lupus nephritis.[78]
6. DNA and other antigens reactive with ANA-containing serum have been demonstrated by immunofluorencence in the deposits within the glomerular basement membrane.[44]

Unlike many antinuclear antibodies that may be found in the serum of patients with a variety of diseases, antibodies to DNA are most often associated with SLE, especially with active renal disease.[71] They may occasionally occur in chronic active hepatitis and are rarely found in the serum of patients with chronic rheumatoid arthritis.[9] On the basis of their frequency of occurrence, alterations in titer with variations in disease activity and their specificity for SLE, DNA-anti-DNA complexes have been imlicated pathogenetically in lupus nephritis. DNA antigen has been found in the sera of patients with SLE[78] before the development of an exacerbation of nephritis and when anti-DNA antibody could not be detected. This suggests that DNA-anti-DNA complexes, formed in antigen excess, may have participated in the production of nephritis. The demonstration of anti-DNA and antinucleoprotein antibodies in eluates obtained from isolated glomeruli treated with deoxyribonuclease (DNAse) which releases antibody previously complexed to DNA,[44] further incriminates the DNA-anti-DNA system in the propagation of renal injury.

Immunofluorescent studies using fluorescein-labeled anti-DNA antibodies demonstrated the presence of DNA antigen within the glomerular basement membrane of affected kidneys, corresponding to the localization of gamma globulins.[44] A summary of the data supporting the role of nuclear antigen-antinuclear antibody complexes in the production of lupus nephritis is presented in Table 2.

In further pursuit of this concept, we have recently performed studies[10] similar to those de-

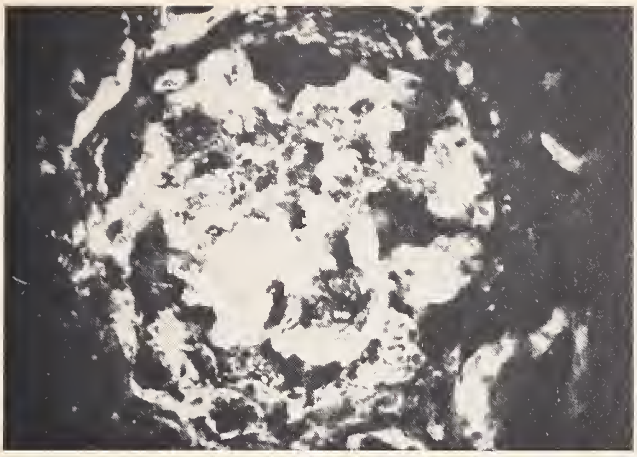

Figure 2.—Section of kidney showing fluorescent granular deposits of immunoglobulin-G within the glomerular basement membrane of SLE kidney (× 250).

scribed. I should like to present some of these data, which are essentially in accord with previous observations.

Immunofluorescent studies were performed on renal tissue obtained by percutaneous biopsy or at autopsy from patients with lupus nephritis. In all instances, granular deposits of gamma-G globulin and beta ${}_1$C-globulin were seen within the glomerular basement membrane and occasional blood vessel walls (Figures 2 and 3). Localization of gamma-M was less frequent and corresponded to the location of gamma-G deposits. Fibrinogen, when present, appeared between focal glomerular loops and within occasional crescents. Glomerular localization of albumin did not occur. Subepithelial electron-dense deposits were present in specimens examined by electron microscopy.

In an attempt to characterize the nature of the intraglomerular immunoglobulin deposits, isolated glomeruli of affected kidneys were eluted with acid buffer or concentrated salt solutions and the eluates were tested for the presence of antinuclear, anti-GBM and other antibodies. ANA's demonstrated by indirect immunofluorescence on human leukocytes, were present in the eluates in greater concentrations than in the corresponding sera. Nuclear fluorescence could be abolished by pretreatment of the nuclear substrate with DNAse.

We then attempted to confirm the localization of nuclear antigens within the immune deposits by staining the tissue with a reagent antibody (FANA) prepared from an SLE serum containing a high titer of ANA including anti-DNA. Direct staining of human leukocytes revealed bright nuclear fluorescence which was partially abolished by pretreatment with DNAse. In order to remove *in vivo* bound ANA, "soft" elutions were performed by incubating the tissues with molar saline at intervals varying from 15 minutes to 3 hours, prior to the application of FANA. Controls included blocking experiments with unconjugated reagent antibody. Bright fluorescence of intrarenal nuclei was observed in uneluted specimens (Figure 4), demonstrating the specificity of the FANA for nuclear antigens. Putative nuclear antigens were demonstrated within the GBM deposits of two lupus kidneys which revealed bright granular fluorescence of antigen reactive with the FANA (Figure 5). Application of DNAse to the eluated specimen prior to incubation with FANA abolished fluorescence in some glomeruli and not in others, suggesting that DNA is but one of a variety of antigens which, in SLE, may participate in the development of com-

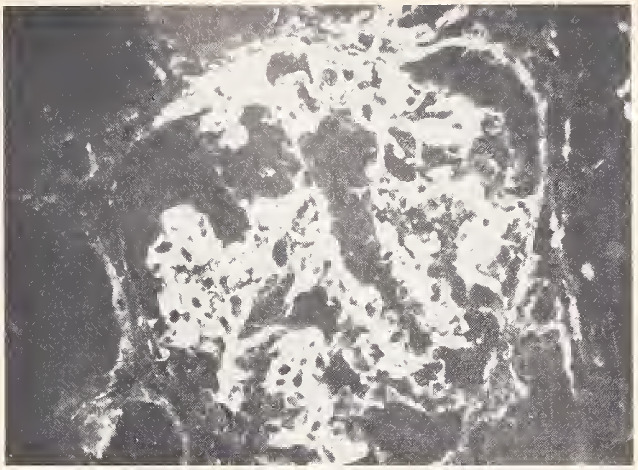

Figure 3.—Glomerulus stained with fluorescein-conjugated rabbit anti-B ${}_1$C-globulin reveals deposits of complement similar to the localization of immunoglobulin (× 250).

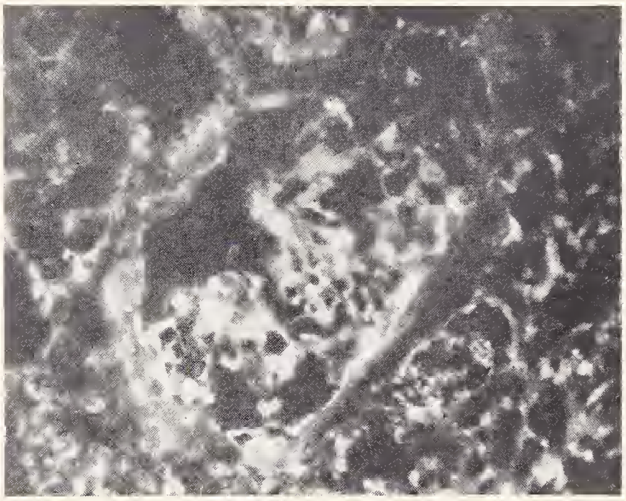

Figure 4.—Staining of uneluted glomerulus by fluorescein-conjugated reagent antibody (see text) reveals bright staining of intrarenal nuclei (× 250).

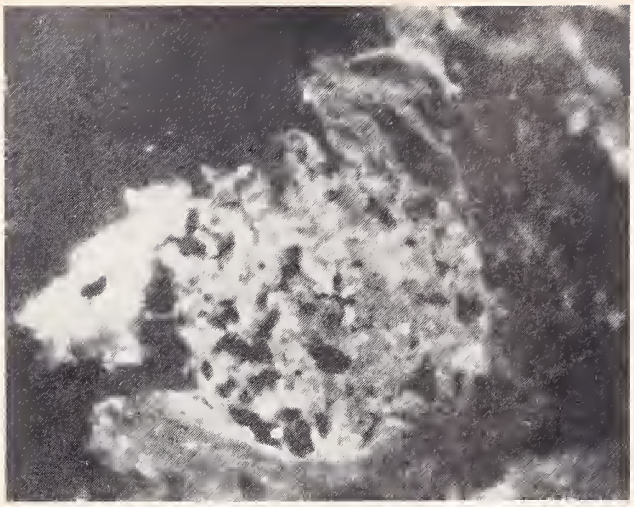

Figure 5.—Fluorescence of putative nuclear antigens seen within the glomerular basement membrane of lupus kidney eluted for 30 minutes and stained with fluorescein-conjugated reagent ANA (× 250).

plex-induced nephritis. Other systems of antibodies and nuclear or cytoplasmic antigens may be involved in the production of lupus nephritis.

In summary, recent investigations have marshalled data implicating immunologic mechanisms in the pathogenesis of lupus nephritis. The causal events resulting in the initiation of these immunologic responses, however, are not known, which provides fertile ground for future investigations.

Serum Cryoprecipitates in Patients With Systemic Lupus Erythematosus

DR. RUNE FORSÉN (Department of Medicine): Cryoprecipitates are frequently found in sera of patients with SLE. Christian and coworkers[13,34] demonstrated the presence of IgG and IgM immunoglobulins, the 11s component of c'1 complement, and alpha-2 macroglobulin in such precipitates. IgA immunoglobulin and other components of complement were identified in some cases. Precipitation appeared dependent upon the presence of the 11s component and IgM possessing antiglobulin activity. Stastny and Ziff[74] found that reprecipitation after fractionation could be demonstrated upon recombination of the IgG and 11s components without the IgM fraction. These investigators also found antinuclear activity of the IgG fraction, which appeared to be less per quantity of IgG than the activity demonstrated in the IgG fraction isolated from the corresponding serum. In a study of nine cryoprecipitates, Lee and Rivero[50] identified the presence of DNA in one case.

The available data have led to speculation as to the possible significance of the cryoprecipitates. An interesting but by no means proven hypothesis is that they may represent circulating immune complexes participating in the genesis of nephritis and other features of the disease.

A study was done on an unselected sample of SLE patients with special attention given to the presence of antinuclear antibodies and DNA in cryoprecipitates. Serum samples were separated at 37°C and refrigerated at 4°C for four days. Cryoprecipitates were isolated and washed four times in cold phosphate-buffered saline solution (pH 7.2). The precipitates were re-suspended in phosphate-buffered saline solution by mechanical disruption and incubation for two hours at 37°C immediately before the various serologic tests. They were incompletely soluble. The identified components and properties of the cryoprecipitates are summarized in Table 3.

Cryoprecipitation occurred in 16 of 18 tested sera from different patients. Precipitated protein was measured by the modified Folin method, showing a range of 31 to 339 μg of protein precipitated per ml of serum.[51] The presence of IgG, IgA, IgM, and the B_1A/B_1C component of complement were tested for, using a double diffusion method against goat antisera specific for these components and with suspensions containing 0.8 to 8.5 mg cryoprotein per ml.[64] Quantitation of IgG, IgA and IgM was performed by a radial diffusion method.[26] Table 3 contains quantitative values for the immunoglobulin content in those instances where sufficient quantity was present. Cases where their presence was only demonstrated by double diffusion are indicated as positive. IgG and IgM were present in all cryoprecipitates. IgA was identified in 11 of 16, and B_1A/B_1C in 7 of 16 samples.

All cryoprecipitates, both heat-inactivated at 56°C and non-inactivated, showed positive Fraction II latex fixation.[30] Because of insufficient material for standardization of concentration, titration was not attempted.

Supernatant sera and cryoprecipitates were specifically tested for the presence of IgG and IgM antinuclear antibodies, using a three-layer immunofluorescent method and a substrate of human leukocytes.[4] The cryoprotein suspensions used contained 0.4 to 4 mg protein per ml. IgG ANA's were found in 10 of 15 supernatant sera, which were tested undiluted, and in 14 of 15 corresponding cryoprecipitates. This suggests that IgG ANA's may have been concentrated in the precipitates in at least four cases, since the cryoprecipitate sus-

TABLE 3.—*Components Identified in Cryoprecipitates from* SLE *Sera*

Patient	*Cryoprotein**	IgG*	IgA*	IgM*	B,A/B,C	ANA		*Diphenylamine Reaction* DNA *Equivalent**	*Reactivity† Assay for* DNA
						IgG	IgM		
J.M.	161	5	+	17	+	+	+	4.1	+
D.W.	80	9	+	23	0	+	+	0	0
C.M.	87	9	+	5	0	+	0	0.3	0
H.M.	122	30	0	13	0	+	+	1.5	0
P.M.	255	32	+	19	0	+	+	0	0
J.G.	55	6	+	21	0	+	+	0	0
B.L.	141	16	5	43	+	+	0	0.5	0
G.T.	339	8	5	21	+	not tested		0	0
M.A.	31	5	0	13	+	+	0	0	0
M.G.	68	6	+	3	+	+	+	1.9	+
B.T.	30	4	0	4	0	+	+	0	0
E.P.	43	6	+	10	0	0	+	0.4	0
B.M.	115	5	8	14	+	+	0	3.4	0
R.A.	71	5	0	+	+	+	+	0.4	0
J.S.	94	22	0	32	0	+	+	0.7	0
C.B.	117	10	1	16	0	+	+	0.5	0

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*μg per ml of serum.

†Reactivity between heat-denatured cryoprecipitate and anti-DNA serum in double diffusion system.

pensions contained considerably less IgG than their corresponding sera. IgM ANA's were apparently demonstrated in 13 of 15 supernatant sera and in 11 of 15 corresponding cryoprecipitates. Since fractionation was not carried out, this may have represented "true" IgM ANA's or an artifact due to IgM antiglobulin attached to IgG ANA's.

The diphenylamine reaction is specific for deoxysugars.[29] Ten of 16 cryoprecipitates were weakly reactive with diphenylamine, a finding of unclear significance, since other substances (such as sialic acid) are also reactive. In order to verify whether this reactivity represented the presence of DNA, the cryoprecipitates were studied in a double diffusion system[76] against a rabbit serum with specific anti-DNA activity produced by immunization of rabbits with methylated bovine serum albumin-DNA conjugates. These anti-DNA sera do not react with oligonucleotides and they react more readily with heat-denatured than with native DNA. DNA was not demonstrable by this method in the cryoprecipitates when tested in their "native" state. After heat denaturation at 100°C for 10 minutes, however, DNA was demonstrable in two cases (J.M. and B.M., Table 3). Another specimen obtained at a different time from patient J.M. was likewise positive. The fact that precipitin lines did not form in the presence of DNAse further verified that the substance identified was DNA.

Our study confirms earlier work showing the constant presence of IgG and IgM in cryoprecipitates from SLE sera; IgA and B_1A/B_1C component of complement were present in some cases. IgG ANA's were frequently found and appeared to have been selectively precipitated in some cases. This is contradictory to the findings of Stastny and Ziff,[74] who found less antinuclear activity per quantity of IgG in the cryoprecipitate than in the corresponding serum. These investigators, however, used the separated IgG fraction for this test, while our study employed whole re-suspended cryoprecipitate. The apparent concentration of IgG ANA's in some cases and the presence of DNA in a few cases allows one to speculate that in some instances a nuclear antigen and an antinuclear antibody may constitute a basic immune complex capable of cryoprecipitation with other cofactors. This hypothesis appears promising enough to warrant further work. The currently available data do not allow any clear correlation between the presence and nature of serum cryoprecipitates and clinical aspects to this disease.

Therapy of Lupus Glomerulonephritis

Dr. Harvey Gonick (Department of Medicine): Dr. Bickel has presented a strong case for the argument that the renal lesion in lupus (SLE) nephritis is immunological in origin, due to the deposition of immune complexes with a subsequent inflammatory reaction.

Our interest in the use of the combination of azathioprine and prednisone in the treatment of this potentially lethal disease was stimulated by the relatively good success in treating the rejection reaction in patients receiving renal homografts, as well as by the preliminary experience of

Michael et al[59] in a pediatric population with immunological renal disease, including five patients who had SLE nephritis.

In order to examine critically the necessity for using cytotoxic drugs in SLE nephritis, it is useful first to review the overall incidence of the renal lesion in lupus as well as some of the available survival figures. Clinically apparent renal disease has been reported to occur in SLE in 46 to 56 percent of all cases.[22,56,70] Autopsy surveys have indicated that the incidence of renal disease is even higher, ranging from 75 to 100 percent.[66]

In recent years it has become apparent that renal disease is the leading cause of death in SLE. In 1964, Dubois[23] reviewed a personal series of 135 cases and found that 34 percent had died of renal disease. This contrasts with earlier reviews in the preantibiotic era, which indicated that infectious disease was a leading cause of death,[43] and in the postantibiotic but presteriod era, when central nervous system disease was a more common cause of death.[21,36]

In an extensive review by Harvey[36] in 1954 of 99 unselected cases of SLE (in which approximately 75 percent of the patients were receiving steroids) it was found that 52 percent of the patients had a four-year survival from the time of diagnosis. In 1956 Dubois[21] analyzed 163 cases of SLE dated from the first appearance of symptoms. His figures indicate a 50 percent five-year survival term on adequate treatment, but only a 50 percent two-year survival on "inadequate treatment," that is, a steroid dose of less than the equivalent of 200 mg of cortisone per day. A review by Meislin and Rothfield[56] in 1968 of 200 cases of adult-onset SLE indicated half of this group had clinically demonstrable renal disease but nevertheless had a 50 percent 20-year survival, whereas the half without clinical renal disease had a 70 percent 20-year survival. These differences in survival rates in several series are difficult to reconcile, but may relate to the severity of the renal lesion. When overt renal disease supervenes, features of ominous prognostic import include the nephrotic syndrome,[67,73] azotemia of even mild degree,[67] and diffuse proliferative glomerular involvement.[70]

Adrenal steroids are frequently effective in treating patients who are acutely ill with active SLE, but their role in established nephropathy is controversial. Early experience[55,73] suggested that steroids were ineffective in nephritis despite suppression of active disease in other systems. Pollak and coworkers[67] observed no consistent correlation between renal and extrarenal activity, but demonstrated improvement and decreased mortality in SLE glomerulonephritis treated with prednisone in high dose (40 to 60 mg daily) for a period of 6 months. These results were looked upon as an improvement over earlier experience of this group with low-dose steroid therapy, that is, the amount sufficient to suppress systemic manifestations of the disease but not sufficient to suppress the renal lesion. This suggestion has been challenged by several subsequent studies, notably a cooperative study headed by Christian,[40] in which an unbiased comparison of high-dose and low-dose steroid therapy indicated no significant difference between these two treatment regimens.

TABLE 4.—*Protocol for Prednisone-Azathioprine Study*

1. Evaluation of effect of combined therapy on patients with SLE nephritis or steroid-resistant nephrotic syndrome associated with glomerulonephritis.
2. Serial study of renal function, morphology and immunological parameters as indices of response to therapy.
3. Azathioprine dosage: 2 to 4 mg per kg daily.
   Prednisone dosage: 30 to 60 mg daily in SLE; 60 mg q.o.d. in nephrotic syndrome.

The histologic features of SLE nephritis have been carefully analyzed by Muehrcke et al[61] and recently reviewed by Comerford and Cohen.[14] Active glomerular lesions include cellular proliferation, wire loops, fibrinoid necrosis, hyaline thrombi, and hematoxyphil bodies. Interstitial abnormalities generally reflect the extent of glomerular damage. Clinical improvement is often accompanied by a corresponding decrease in histological activity.[67] Both adrenal steroids[67,72] and cytotoxic agents[59] appear to reduce the cellular component of the glomerular response in SLE, but basement membrane abnormalities are frequently unchanged.

Table 4 indicates the protocol we have used in following patients with immunological renal disease. Our intent was to study the effect of combined therapy (that is, azathioprine and prednisone) in patients with SLE and glomerulonephritis with steroid-resistant nephrotic syndrome. All patients had serial studies of renal function, morphology and immunology following therapy. Percutaneous renal biopsy was performed before treatment was begun, and was repeated at 6-month intervals. Biopsy specimens were divided for light and immunofluorescent microscopy. Glomeruli were stained for IgG, the beta $_{1}$C-globulin component of complement, and fibrinogen. Changes in

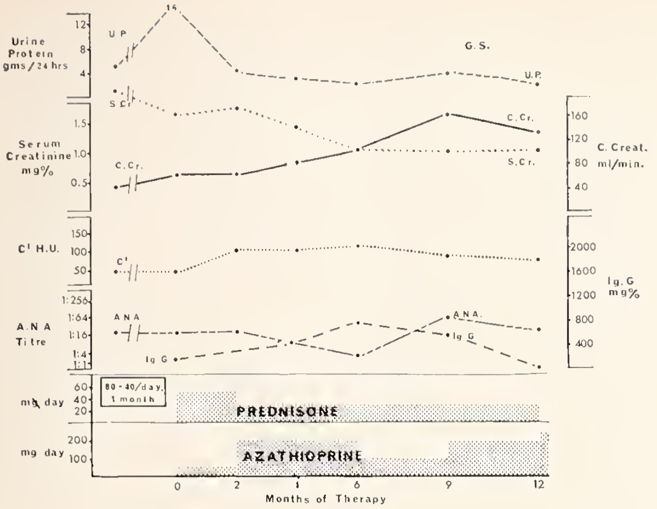

Chart 2.—Clinical course of patient G.S. (Table 5) following treatment with prednisone and azathioprine.

light and immunofluorescent specimens were graded on a semi-quantitative basis for later analysis. Renal function studies included measurements of creatinine clearance, ^{125}I-iodothalamate clearance, urine protein excretion, and Addis counts. Immunological studies included ANA, quantitative immunoglobulins, total serum hemolytic complement (C′), and beta $_1$C-globulin (C′3). The functional and immunological studies were performed before therapy was begun and then at 2- to 4-week intervals. Azathioprine was used in a dose of 2 to 4 mg daily, more commonly in the lower dose range. Patients with lupus were treated with 30 to 60 mg of prednisone daily, whereas patients with glomerulonephritis were treated with 60 mg every other day.

Chart 2 indicates the clinical course in a typical patient, this one a 17-year-old Caucasian male who presented with a 4-month history of fever, arthralgias, hypertension, and anasarca due to severe nephrotic syndrome. He had not responded to prednisone in a dose range of 40 to 80 mg per day for one month before the initiation of combined therapy. Within 6 months there was a decided clinical improvement associated with a rise in glomerular filtration rate and reduction in proteinuria. Serum complement rose to normal and ANA titers fell (but rose again subsequently despite continued clinical improvement). Pretreatment biopsy showed severe, diffuse membrano-proliferative glomerulonephritis with some localized necrosis. Immunofluorescence revealed a typical granular deposition of IgG and beta $_1$C along the glomerular capillary membranes. Following treatment there was pronounced diminution in the proliferative changes as well as in the amount of IgG and beta $_1$C deposition.

Table 5 lists the overall results obtained in 14 patients with SLE who had been on treatment for at least 6 months as of June 1968. It should be emphasized that two of these patients (N.M. and S.B.) had severe azotemia with creatinine clearances of 10 and 12 ml/min. Since four other patients had mild azotemia, it is apparent that we are dealing with a group which would be expected to have a poor prognosis. In addition, nine patients were nephrotic, again a poor prognostic sign.

Serum complement was depressed in eight of twelve patients before therapy and rose in seven of these eight following therapy, correlating relatively well with functional and/or morphologic improvement. ANA titer, on the other hand, was low or even absent in four patients with biopsy-proved glomerulitis. When initially elevated, ANA titer usually fell, but the decrease did not correlate with changes in functional measurements. Immunoglobulin-G levels were unpredictable. Some patients with relatively low values had heavy proteinuria and it is possible that they were losing large quantities of immunoglobulins in the urine. Subsequent data, however, have demonstrated that IgG synthesis is depressed by azothioprine.* When IgG levels before therapy were elevated, successful treatment was usually associated with a fall in IgG to normal. Immunofluorescence frequently decreased, but there was not always a good correlation between diminution in immunofluorescence and other gauges of progress. Histologically, the most impressive change was a decrease in glomerular cellular proliferation, seen in 10 of 14 patients.

Complications were relatively frequent on combined therapy (Table 6). Two patients died of infections, one from Gram-negative sepsis following deep abscesses of thighs and buttocks, and one from subarachnoid hemorrhage incident to probable bacterial meningitis. Hypercorticism appeared in 12 patients, while hyperglycemia developed in three and three others became emotionally disturbed. Hepatotoxicity was not seen in these lupus cases but has been noted in patients with glomerulonephritis and nephrotic syndrome treated on a similar protocol.

In summary, it would appear that the combination of azathioprine and prednisone is a promising

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*Levy, J., Barnett, E. V., McDonald, N. S., and Klinenberg, J. R.: Reduced IgG and IgM synthesis with azothioprine therapy, Arthritis Rheum., Dec. 1969, in press (abstract).

TABLE 5.—*Results of Combined Therapy in* SLE *Nephritis*

Patient	GFR	*Urine Protein*	ANA	C′	IgG	*Pathology (Proliferation)*	*Immuno-fluorescence*	*Months Rx*
V.S.	inc.	dec.	dec.	inc.	dec.	n.c.	dec.	12
H.K.	inc.	dec.	dec.	n	dec.	dec.	dec.	12
N.A.	n.c.	dec.	dec.	inc.	. .	dec.	dec.	21
D.M.	inc.	dec.	n.c.	low—n.c.	inc.	dec.	dec.	12
M.A.	inc.	dec.	dec.	inc.	inc.	dec.	dec.	6
E.S.*	dec.	dec.	dec.	inc.	dec.	n.c.	dec.	6
E.P.	inc.	dec.	dec.	inc.	inc.	dec.	. .	6
A.B.	n.c.	dec.	dec.	. .	. .	dec.	. .	27
G.S.	inc.	dec.	dec.	inc.	inc.	dec.	dec.	13
N.M.	dec.	n.c.	dec.	. .	. .	dec.	. .	30
R.A.	n.c.	dec.	n.c.	n	n.c.	n.c.	n.c.	6
R.G.*	n.c.	inc.	dec.	inc.	dec.	n.c.	inc.	12
N.M.†	n.c.	n.c.	n	n	n.c.	dec.	inc.	7
S.B.†	dec.	n.c.	dec.	n	n.c.	dec.	. .	7

Inc.: Increased; Dec.: Decreased; n c.: No change; n: Normal.
*Died of infection. †Died of uremia.

TABLE 6.—*Complications of Combined Therapy*

Total number of patients on Rx	14
Hypercorticism	12
Infections	4
Hyperglycemia	3
Mental disturbances	3

means of therapy in patients with lupus nephritis, but is not without hazard. A definitive evaluation of the role of this drug combination, however, requires more prolonged observation as well as comparison of effectiveness and toxicity with a matched series of patients treated with each drug independently.

Discussion

DR. BARNETT: What have we accomplished in our attempts to define the cause and cure of diseases in a group of patients that we have labeled as having systemic lupus erythematosus? We have obviously not found the cause or cure as yet. We have spun off a great deal of information of scientific import and we have trained a number of scientists in the attempt.

From Dr. Kantor's presentation it is apparent that we can distinguish systemic lupus erythematosus in certain patients from rheumatoid arthritis in other patients who have similar serologic abnormalities and similar clinical manifestations. On the one hand, SLE patients frequently have glomerulonephritis and rarely have articular erosions, while RA patients show the converse. In our experience, this is a more important distinction than any serologic test. We do know, however, that in untreated patients the absence of antinuclear antibodies practically excludes the diagnosis of systemic lupus erythematosus.

Dr. Bickel has reviewed the evidence incriminating immune complexes in glomerulonephritis. Our work[2] has made us particularly receptive to the hypothesis that "nuclear" antigens and antinuclear antibodies participate in such complexes. However, the evidence accumulated so far is too scanty and there are still too many gaps and contradictions. Nuclear antigens in small amounts are present in normal sera.[3,7] Circulating complexes have been detected without associated glomerulonephritis or hypocomplementemia and the role of DNAse and DNAse inhibitors is unclear. Current investigations at many centers promise to clarify the matter.

As was suggested by Dr. Forsén, the presence of cryoglobulins may be an indication of circulating complexes. Antigens and antibodies when mixed *in vitro* will precipitate much better at reduced temperatures. This may explain what happens when we place a patient's serum in the refrigerator for 4 days and obtain a precipitate containing a variety of ingredients. Dr. Gonick reviewed our experience in the therapy of lupus glomerulonephritis with combinations of prednisone and azathioprine. Does such a therapeutic trial give us insight into the cause of the disease or its pathogenesis? Since these drugs have multiple pharmacologic actions, such insight has not been forthcoming. These drugs are "anti-inflammatory"; they affect cells that invade the lesion; they affect antibody production; they are antiviral agents and affect the mediators of inflammation.

The Etiologic Significance of Similar Abnormalities in Diseases of Man, Mink, and Mouse

If there are similar abnormalities in diseases of man and of lower species, what interpretation can be made? The serologist studying human disease is frequently confused by the similar abnormalities in tertiary syphilis, leprosy, and subacute bacterial endocarditis. These are human diseases of known and divergent cause, but the serologic similarities apparently reflect similar pathogenetic mechanisms.

Aleutian minks are of a strain developed because of its attractive metallic blue pelt. It was found that such minks of genotype Aa did not reach adult life but died with hepatitis, vasculitis, glomerulonephritis and hyperglobulinemia, and some even with monoclonal spikes resembling myeloma proteins.[68] To complicate matters, it was found that this disease could be transmitted by ultrafiltered material, less than 50 mμ in size, to minks of other strains, to the heterozygotic Aa minks, and even to ferrets.[42] The veterinarians were thus confronted with an economically important disease that appeared immunologic on the one hand, and infectious on the other.

We were pleased to have the opportunity to study the sera of heterozygotic Aa minks that acquire the disease spontaneously and only late in life.[8] These Aa minks were given ultrafiltrates of highly infectious spleen material, and 10 weeks later 100 percent had evident disease. We were sent serum specimens before the innoculation of the infectious material, and serum specimens collected 10 weeks later in the presence of obvious disease. Utilizing the sorts of antisera described by Dr. Forsén, we could find antigen in small amounts and low incidence in sera before the development of Aleutian disease (Table 7) and in large amounts and higher incidence in the presence of Aleutian disease. ANA's detectable by immunodiffusion, precipitin tests in dilute agarose with single-strand calf thymus DNA were detected only in sera from minks with overt disease. ANA's detectable by the more sensitive immunofluorescence technique using human leukocyte nuclei as antigens were detected before overt disease developed, but were detectable in higher titer and greater incidence in the presence of the disease.

Sera were collected from Aa minks that acquired the disease spontaneously in later life. They had large amounts of antigens detectable by anti-DNA antibodies and they had a high incidence of antibody to single strand DNA. Aa minks from different mink farms with low incidence of spontaneous Aleutian disease but with the same genetic susceptibility to this disease did not show these abnormalities.

TABLE 7.—*Incidence of "Nuclear" Antigen and Antinuclear Antibodies in Experimentally Induced Aleutian Disease* (AD)

	*Pre-AD** *Percent*	*Post-AD†* *Percent*
Antigen content by precipitin tests	38	50
ANA by precipitin tests	0	95
ANA by immunofluorescence	35	100

*Sera obtained before disease.
†Sera obtained at time of evident disease.

The results of our studies on the sera of New Zealand black (NZB) mice were very similar to the results obtained with Aleutian mink sera. New Zealand black mice are well known to have a high incidence of hypergammaglobulinemia, hemolytic anemia, nephritis and antinuclear antibodies. We recently demonstrated that sera from these mice have a high incidence of precipitating antibodies to single-strand calf thymus DNA, and nuclear antigens are frequently demonstrable as well.[81]

The antigens found in sera from persons with SLE, from minks with Aleutian disease, and from NZB mice can be detected by a variety of anti-DNA antibodies (Table 8).[81] In some cases the nuclear antigens appear resistant to DNAse. Since the immunodiffusion studies demonstrate that the nuclear antigens show either complete or partial identity with single-strand calf thymus DNA, they apparently have purine and pyrimidine determinants. The relative resistance to DNAse may be attributable to the binding of the antigens by ANA present in the specimens.

Our immunodiffusion studies to date make it appear unlikely that the nuclear antigens in these three conditions are identical.

Antinuclear antibodies are found in all three situations. Among these ANA's we have consistently detected antibodies to single-strand DNA. Does this suggest that the primary immunogen in these three situations is a "denatured" DNA or single-strand DNA virus? In all three situations there is hypergammaglobulinemia, vasculitis and nephritis. In systemic lupus erythematosus there is mild arthritis, and in all three conditions the role of immune complexes in pathogenesis has been in-

TABLE 8.—*Comparison of Systemic Lupus Erythematosus, Aleutian Disease and the Disease in* NZB *Mice*

Factor	SLE	AD	NZB
"Nuclear" antigens in sera	rare	frequent	rare
Antinuclear antibodies	frequent	frequent	frequent
Antibodies to SS DNA	frequent	frequent	frequent
Hyperglobulinemia	frequent	frequent	frequent
Vasculitis	frequent	frequent	frequent
Nephritis	frequent	frequent	frequent
Arthritis	mild	absent	absent
Role of immune complexes in pathogenesis	incriminated	incriminated	incriminated
Infectious	?	yes	in controversy
Genetic factors	in controversy	present	present

criminated.[5] Persistent infections of mice with lymphocytic choriomeningitis virus or lactic dehydrogenase virus has been associated with immune complex disease with these clinical characteristics. The prevalence of antibodies to single-strand DNA in SLE, Aleutian minks and mice has encouraged us to pursue serologic studies on the possible role of small DNA-containing viruses (picodnaviruses).[5,54]

That Aleutian disease is caused by an infectious process appears well documented by the transmittability of the disease by ultrafiltrates. This may also be the case for the disease in NZB mice. Surprising electron microscopic observations[62] recently have been added to evidence that systemic lupus erythematosus is of viral origin. The susceptibility of certain strains of minks and mice indicates genetic predisposition to the infectious agent. Epidemiologic studies in SLE are also consistent with the combination of genetic susceptibility plus an inciting agent.

It is particularly uncomfortable for scientists experienced in data collection from well controlled experiments to deal with data suggesting multifactorial etiologic agents. The clinical investigator studying systemic lupus erythematosus must now consider the possible interrelationships of autoimmunity, immune complex disease, persistent infection and genetic susceptibility.

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EDITORIAL

Medicine and the 1970s

MEDICINE ALONG WITH THE NATION and the world is about to enter a new decade. It seems certain that the 1970s will be at least as shattering to tradition as were the 1960s. There is bound to be change and much of it fundamental. Depending upon one's outlook what lies ahead may be viewed with anticipation or foreboding, or perhaps a little of each.

The decade now just closing has seen widespread challenge to and even rejection of many of the traditional attitudes and values which have long been bulwarks of American and indeed Western society. There have been substantial inroads upon long accepted standards of public and private morality as this nation has hitherto understood them. The established order of many churches, the military and even the law has been more or less successfully attacked. The educational system, both public and private, has been exposed as curiously vulnerable to intellectual and physical confrontation and surprisingly ill-fitted for adaptation or change.

Medicine has by no means escaped criticism. The established approach to health care delivery was all but shattered during the 1960s by far-reaching federal legislation. The medical profession was singled out for particular attack and vilification in the press and elsewhere, and at the end of the decade remains a convenient whipping boy. But in spite of all the attacks and public abuse heaped upon the profession, the public opinion polls continue to indicate that physicians and even organized medicine stand very high in the public esteem. Perhaps this in part at least reflects the dramatic achievements of medical science. In any case the thrust of the attack on health care was not so much to tear down as to try to create something better.

The 1970s will surely be different. Some way will be found to end the kinds of disorder and destruction which in the long run cannot be tolerated by any society, especially when those who are tearing things down have nothing to propose. There will be new values which will find acceptance to replace those which are being rejected. There is much to suggest that at least some of these new values will be based upon what is known of human biology, that is, the realities of human nature and human behavior. This will occur as modern society inevitably comes to grips with what must be done to achieve health and well-being for individual citizens and indeed all of the humanity encased in this closed and seemingly shrinking biosphere from which there is no practical escape either now or in the future.

It is entirely possible that the 1970s will mark the beginning of a new cultural recognition of the biologic nature of human society in much the same way that the biologic nature of man himself was finally recognized toward the end of the last century. Medicine, which applies what is known in the human biology of health and disease to promote health, well-being and survival not only of the individual but of the species, should have an important and exciting role to play. Physicians may look to the 1970s with anticipation, certainly not foreboding. We may well be at the threshold of a new era in the history of human society.

Systemic Lupus Erythematosus

FOR OVER HALF A CENTURY systemic lupus erythematosus (SLE) was considered a rare and fatal disease. During the 1930s suspicions arose that hypersensitivity might be involved in pathogenesis. In 1948 the LE cell was discovered. In the 1950s the application of immunological techniques in the study of SLE led to the identification of autoimmunity in man, and established that the formation of LE cells is an immunological event. In succeeding years the use of diagnostic immunological techniques has led to the recognition of an extraordinarily broad spectrum of clinical forms of SLE affecting many different major organ systems with intensities from mild to fulminating.

During the same period, the discipline of immunology has rapidly matured. Transplantation immunology has emerged, and with it a recognition of the phenomenon of immunological tolerance which is a state of unresponsiveness to antigen antithetical to classical sensitivity. The cellular events which constitute the immune response have at least in part been identified and thereby the sequential components of that response have been opened for study. Much of the molecular structure of antibody is now known. The role of individual genotype in governing the immune response is being established. Autoimmunity has become a recognized component of diseases in fields as previously separate as Rheumatology, Endocrinology, Gastroenterology, and Neurology.

Matters have progressed further. It is now well established that autoantibodies to a tissue can in certain instances protect that tissue from immunologically induced disease. Certain types of viral infections are apparently harmless until host defenses come into play; then the cellular protection responses damage host tissue and produce disease. These two phenomena suggest that what would be expected to be harmful may be helpful in certain circumstances, and vice versa. Furthermore, states of immunological sensitivity and tolerance can coexist in the same animal, with first one and then the other predominating. The immune response of the whole animal is malleable. The implications of this flexibility as it affects the intensity, quality, and reversibility of immune responses are only beginning to be understood.

The conference from UCLA on Systemic Lupus Erythematosus, published in this issue, illustrates many recent advances and underscores many current problems in clinical immunology. It is now possible to identify multiple variations of the classical clinical categories of rheumatic disease and to observe one evolve into another. It is also possible to identify specific immunological events accompanying certain types of disease, such as the association of autoantibody to DNA with nephritis. The converse association, involving the protective effect of certain autoantibodies, has also been established in experimental disease and suggested in SLE. In experimental animals, analogues of autoimmune hemolytic anemia and SLE arise naturally in strains with particular genotypes as a product of aging or possibly viral infection.

We still do not understand, however, the associations of particular serological abnormalities with patterns of clinical disease, the variations in serological patterns which accompany transformation of one clinical form into another, or even the natural history of most variants of SLE. We have only very modest knowledge of the mechanisms of tissue damage. It remains very difficult to establish an appropriate prognosis for individual patients or to decide with accuracy the type and intensity of treatment which is needed.

The current treatment of immunological diseases further emphasizes our ignorance. Corticosteroids have enjoyed widespread use in the treatment of these diseases since the early 1950s. Experience establishes beyond doubt that they can terminate the lupus crisis. However, there still does not exist a single controlled study demonstrating conclusively the benefit of these agents. Their comparative utility in different forms of SLE and related diseases is also unresolved. Recently it has become popular to use cytotoxic agents, particularly in the treatment of patients who appear resistant to corticosteroids. The rational is sound: Cytotoxic agents inhibit the primary immune response, reduce the secondary response, interfere with cellular hypersensitivity, diminish inflammatory reactions, facilitate the induction of immunological tolerance in certain settings and impede the development of experimental immunological disease. However, the clinical literature on the use of these agents contains only reports of treatment of small numbers of patients and uncontrolled evaluations. Some clinical evidence has been presented suggesting that a combination of corticosteroids and cytotoxic agents is superior to either type of agent alone, but here too the data are not rigorous. Preliminary controlled investigations suggest that the cytotoxic drugs alone are often ineffective in influencing immunological disease. Furthermore the price paid by patients receiving combined therapy is very high in terms of opportunistic infections which have become a frequent cause of serious morbidity and death.

The discussion from UCLA serves to emphasize the needs for the next few years. These include careful clinical observations (1) to establish the natural history of various forms of SLE, (2) to identify rigorously the patterns and significance of different serological reactions in relation to pathogenesis, prognosis and response to therapy and (3) to determine the efficacy of various treatment programs. The influence of patient genotype and of viral infection on susceptibility to immunological disease requires definition. Study of mechanisms of tissue damage may be difficult in man but animal models now provide appropriate subjects for investigation. It should be possible, once these mechanisms are identified, to design specific therapeutic programs to counteract them. The flexibility and adaptability in the immune response make such therapeutic manipulations more than a distant hope; if autoimmunity results from a loss of natural tolerance, perhaps we can discover biological ways to reestablish that tolerance.

The conceptual and methodological tools are at hand to accomplish these objectives. In the past, the study of human disease has provided a great portion of the impetus for the growth of the discipline of immunology. We may hope that more rigorous study of human disease will now yield both improved care of patients and an even greater increment in knowledge of the human immune response.

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Polymyalgia Rheumatica

AMERICAN PHYSICIANS have been slower than those in Britain to accept polymyalgia rheumatica as a distinct clinical syndrome. Perhaps it is less common in North America than in Europe. Nevertheless, once a case is recognized others seem to appear and the incidence may not differ greatly on the two sides of the Atlantic Ocean. In any event, the incidence if it be different has not attracted the attention of epidemiologists.

A more immediate problem, because it has important clinical implications, is the relationship of polymyalgia rheumatica to the syndrome of giant cell arteritis. That name is slowly gaining favor over the terms *temporal* or *cranial* arteritis because it is clear that on occasion the disease can affect any part of the aorta or its branches.

There is general agreement that the musculoskeletal symptomatology of polymyalgia rheumatica and giant cell arteritis is the same and that patients ultimately proven to have giant cell arteritis may have a prodrome of polymyalgia for several years before arterial changes become evident.[1] Unfortunately, it has been well documented that blindness or a serious cerebrovascular accident may be the first manifestation of the arteritis.[2]

Both polymyalgia rheumatica and giant cell arteritis are dramatically improved by corticosteroid therapy. So striking is the response of the former, even to small doses, that the therapeutic effect has been proposed as a diagnostic test. Larger amounts, however, may be required to control the manifestations of giant cell arteritis, and the frequency of complications, especially osteoporosis in the elderly population characteristically affected, becomes a major concern.

Both diseases tend to have self-limited courses extending over a few months to a year or two, but relapses may occur[3] and there is no established means of knowing when therapy can be stopped. The author knows of three patients with temporal arteritis who have suffered vertebral compression fractures while on therapy, in one case after only a few months of treatment and in another after attempts over 2 years to reduce the dose of steroid had been frustrated by the reappearance of symptoms. One is, therefore, reluctant to accept immediately the recommendation that since any patient with symptoms of polymyalgia rheumatica may develop serious manifestations of giant cell arteritis, all should be treated with corticosteroid from the outset. This recommendation obviously depends on the supposition that all patients with polymyalgia rheumatica either have giant cell arteritis from the start or are in danger of developing arteritis. It is agreed that the musculoskeletal symptoms are indistinguishable. Muscle biopsy usually shows no pathology,[4] the vessels involved by giant cell arteritis being larger than those found in muscle. Another approach has been to perform routine temporal artery biopsy when the diagnosis of polymyalgia rheumatica is made. The procedure is a benign one and is certainly indicated when the temporal arteries are found to be tender or thickened and pulseless. However, biopsy specimens showing active or healed temporal arteritis have been obtained from arteries which were clinically normal.

Temporal arteriography has recently been proposed as a better screening procedure and should certainly help to define the area from which to take specimens for biopsy.[5] It is a fact, unfortunately, that in some patients who develop catastrophic consequences of giant cell arteritis the temporal arteries are never involved.

An autopsy study of the temporal arteries of 39 elderly persons without recorded symptoms of polymyalgia rheumatica or giant cell arteritis demonstrated lesions consistent with healed arteritis in two.[6] Moreover, both died possibly as a result of arteritis. If carried to the extreme, an argument could be made for investigating the temporal arteries of all elderly persons and at least anyone found on questioning to have fatigue, muscle soreness, headache or any of the vague symptoms which may be a part of the syndromes under discussion. Clearly some middle ground must be found. The absence of normal pulsation in a temporal artery is certainly not conclusive evidence that it is affected by giant cell arteritis, for pulsation may be absent in one or both arteries in 5 percent of middle aged and elderly adults attending an arthritis clinic.[7]

In the final analysis, most physicians would administer corticosteroids to patients with polymyalgia rheumatica who developed headaches, face or scalp pain, or cerebrovascular symptoms of any kind with or without a positive biopsy or arteriogram. Those who do not have such symptoms should probably have one or another procedure performed to demonstrate giant cell arteritis and should be treated if the result is abnormal, whatever the clinical symptoms.

As for the remainder, the physician must be prepared to make a somewhat arbitrary decision based on whatever evidence he finds compelling. Some patients cannot be freed of their disabling muscular complaints by anything other than corticosteroid. The situation is not an unfamiliar one in medicine.

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Whither Nursing?

THE DICTIONARY defines a nurse as "a person skilled in caring for and waiting upon the infirm, the injured, or the sick; specifically: one especially trained to carry out such duties under the supervision of a physician."* Thousands of young girls, and some young men, have been drawn to a career in nursing by this ideal of personal service, under competent direction, to someone who is afflicted or suffering. Nurses and physicians have thus shared similar attitudes and have worked closely together as a team. The nursing profession has traditionally been held in a kind of preferred status by physicians. The atmosphere has usually been peaceful and much of the time the relationship idyllic.

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*Webster's Third New International Dictionary of the English Language—Unabridged.

Recently there are signs that things have begun to change. The traditional more or less all-purpose nurse who at once served as assistant to a physician and attendant to a sick patient has begun to undergo differentiation and she now performs a myriad of specialized functions which may have little or nothing to do with "waiting upon the infirm, the injured, or the sick, under the supervision of a physician." Already there are surgical, psychiatric, intensive care, public health, coronary care, school, office, and administrative nurses, all with special skills. The varieties of nurse specialists are growing in number and importance. Increasingly many of these specialized nurses are being expected to make independent decisions affecting the care of patients, decisions which often must be made in situations quite remote from the immediate supervision of a physician, if indeed there is a supervising physician.

One important and perhaps inevitable result of this specialization is that the nurse has started to drift away from her role as attendant to the patient and has begun to stand more closely with the physician as an assistant, associate or even colleague. As a consequence of this, traditional nursing with its traditional satisfactions is being more and more left to others while the nurse in her new role has yet to be fully accepted as an actual colleague of the physician.

Perhaps this trend may be a root cause of some of the things that are now happening in nursing. But whatever the cause, there are clear signs of some kind of an identity crisis in the nursing profession. We see nursing leadership making very considerable efforts to identify and define what is now to be the role of nursing. There seems to be a driving compulsion to upgrade the status of nursing. The recent bold use of strike tactics with the tacit assistance if not the formal support of a well-known and powerful labor union was considered by many to be very much out of character for this gentle and beloved profession.

It seems more than likely that storm signals will appear along the course upon which nursing is embarked. It is suggested that certain apparent fallacies will lead to some difficulties. For example, it seems inconsistent to promote the professionalization of nursing on the one hand and on the other to use tactics which in the view of many serve only to deprofessionalize it. It seems unrealistic to expect to retain the role of bedside nurse and at the same time price the services of a registered nurse substantially beyond what patients can afford in ordinary circumstances. And one may question the ultimate result of what seems to be the efforts of the nursing leadership to create an artificial new administrative role for the nurse in the health care delivery system (particularly in the hospital setting), to force the acceptance of that role by the use of pressure, and then expect the health care economy to support it with some generosity. This appears to be what is occurring, as nearly as one can glean from a perusal of the recent nursing literature and from a rather careful observation of recent strike tactics employed by the nursing profession in California. If this assessment is anywhere near accurate there will not only be storm signals but some quite heavy weather ahead.

If the problem can correctly be viewed as fundamentally an identity crisis, then it should be dealt with as quickly and reasonably as possible. Perhaps the time has come to admit that the specialized registered nurse of today and tomorrow really will no longer be a nurse in the traditional sense, and will more than likely be lifted out of the traditional nursing role to take her place among a new order of physician assistants or physician associates. Perhaps medical associates would be a better term. The need for such an order of well trained health personnel with various and differing skills is becoming increasingly apparent. So far there has been little discussion of the nature of such a new order, but clearly old-fashioned nursing would not be its dominant concern. This new category of professional specialists should stand closely with the physician and share his responsibilities for patient care and for community, environmental and species health care. Men would play an equal role with women. Those who achieved this new status might become recognized as "professional associates in medicine" or given some similar designation commensurate with their training and responsibilities within what is now coming to be called the health team. Traditional nursing would then be left to the new categories of nurses who are already beginning to occupy the field.

Perhaps this will be an answer to "whither nursing?"

PRE-EXISTING SICKNESS - HEALTH INSURANCE

There Is A Difference

Some health insurance is written as group insurance and others as individual or family insurance. Entirely different principles prevail. Since the physician often helps his patients deal with insurance, an understanding of this is necessary.

HBA Life offers both group and individual or family policies. In 1944, HBA was one of the early pioneers in offering individual or family health insurance. At that time, Blue Cross and most insurance companies were not willing to write insurance other than group. The company is also proud of being one of the early pioneers in guaranteed renewable health insurance. Even today the company still ranks nationally among the top 40 companies in volume of individual guaranteed renewable insurance. Most companies, and many still do, wrote health insurance as renewable only at the option of the company. Thus, when people became a bad health risk, their insurance could be taken from them.

Group or Individual-Family

State insurance law requires that groups be at least ten employees of the same employer or 25 or more participants of the same trade association. Usually a requirement is made that at least 70% to 80% of the group enroll to prevent selection of risk against the company. With these provisions, the group insurance can be issued to cover conditions from the time the insurance starts. While there may be some people needing health care at the time, others in the group will be good risks. The law of averages, rather than a selection of risk, therefore, protects the company.

On individual or family policies there is always a certain number of these people who only decide to obtain insurance at the time they are not feeling too well. Therefore, there is a certain risk selection against the insurance company to investigate and evaluate. Sometimes health information is not obtainable by the company particularly if the people did not answer the questions on the application honestly.

A company can't afford to pay for a long needed operation for someone who just took out insurance a few weeks or a few months ago. Otherwise, no one would need to take out insurance until they were ready to go to the hospital.

The company has the right (for three years) to further investigate at the time of a claim to see if the facts given them by the applicant for insurance were correct and if the cause of this sickness did commence after they had the policy. All policies of insurance are issued in consideration of the payment of the premium and of the application. If the application misrepresented or gave fraudulent information or lack of information, a contract of insurance did not exist and the company need merely refund the premium payment.

All health insurance issued by HBA is either Guaranteed Renewable for Life or to age 65 or eligibility for Medicare. In other words, the company cannot cancel the insurance or change the terms of the contract. It is, however, necessary that the people pay the premiums by the due date or within the grace period or they, themselves, cancel the contract.

When the premium payment for insurance is after the grace period, it is then subject to reinstatement. In other words, the applicant must reapply and the company must decide whether or not to again accept the risk. Here again the company has the right, during the contestable period, to rely upon the accuracy of the statements. Companies must realize that some people intending to drop a policy quit making premium payments and then if, a few months later, they are not feeling too well, decide maybe they better get their insurance back. To keep premium rates in line, the company must protect itself.

Some people take out individual or family policies because they are not eligible for group coverage. Others take it out and wish to have a guaranteed renewable policy so they will have insurance regardless of change of employment. This way they know they will always have coverage available whether they decide to go into business for themselves or accept other employment. Good individual and family health insurance is available to those in ordinary good health.

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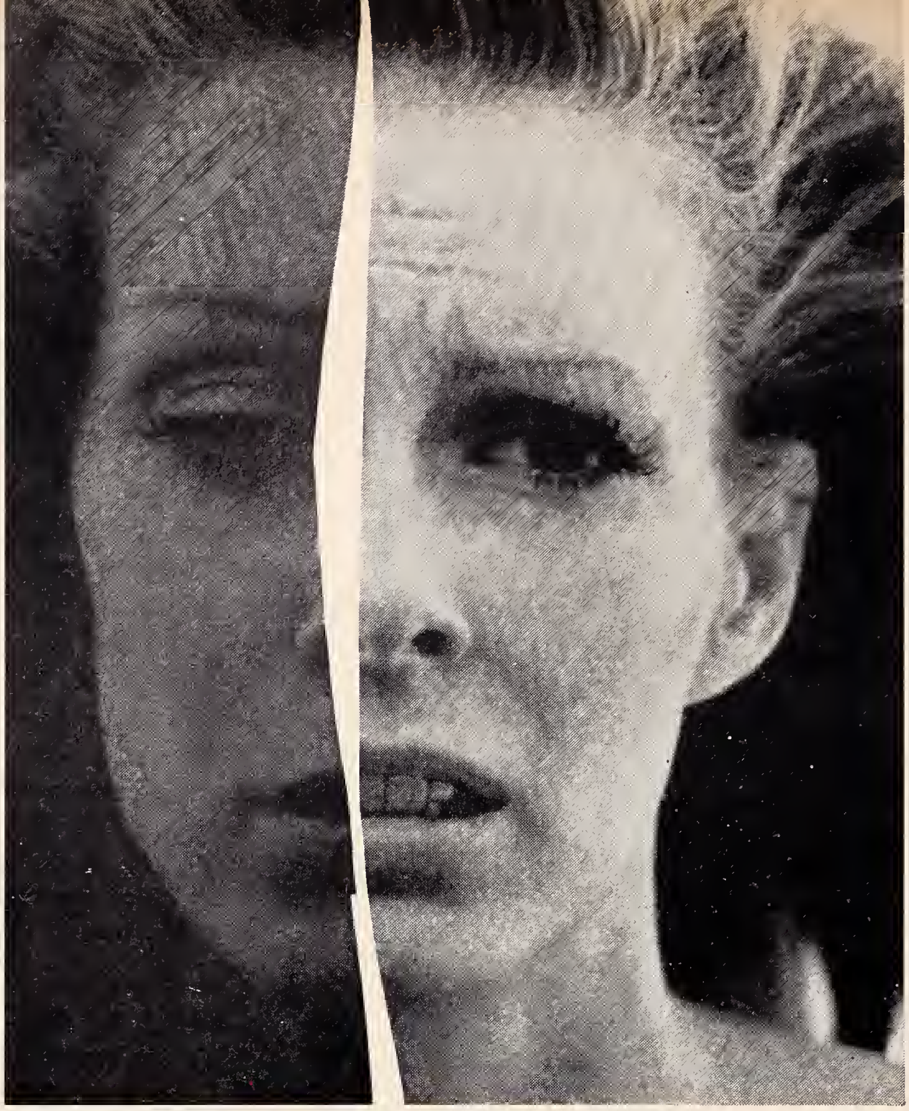

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Before prescribing or administering, see Sandoz literature for full product information, including adverse reactions reported with phenothiazines. The following is a brief precautionary statement.

Contraindications: Severe central nervous system depression, comatose states from any cause, hypertensive or hypotensive heart disease of extreme degree.

Warnings: Administer cautiously to patients who have previously exhibited a hypersensitivity reaction (e.g., blood dyscrasias, jaundice) to phenothiazines. Phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus insecticides. During pregnancy, administer only when necessary.

Precautions: There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures. In epileptic patients, anticonvulsant medication should also be maintained. Pigmentary retinopathy may be avoided by remaining within the recommended limits of dosage. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving). Orthostatic hypotension is more common in females than in males. Do not use epinephrine in treating drug-induced hypotension. Daily doses in excess of 300 mg. should be used only in severe neuropsychiatric conditions.

Adverse Reactions: *Central Nervous System*—Drowsiness, especially with large doses, early in treatment; infrequently, pseudoparkinsonism and other extrapyramidal symptoms; nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. *Autonomic Nervous System*—Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. *Endocrine System*—Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. *Skin*—Dermatitis and skin eruptions of the urticarial type, photosensitivity. *Cardiovascular System*—Changes in the terminal portion of the electrocardiogram have been observed in some patients receiving the phenothiazine tranquilizers, including Mellaril (thioridazine). While there is no evidence at present that these changes are in any way precursors of any significant disturbance of cardiac rhythm, several sudden and unexpected deaths apparently due to cardiac arrest have occurred in patients previously showing electrocardiographic changes. The use of periodic electrocardiograms has been proposed but would appear to be of questionable value as a predictive device. *Other*—A single case described as parotid swelling.

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References: 1. Coodley, E. L.: Curr. Ther. Res. 4:460 (Sept.) 1962. 2. Johnson, H. J., Jr.: Penn. Med. J. 67:35 (May) 1964.

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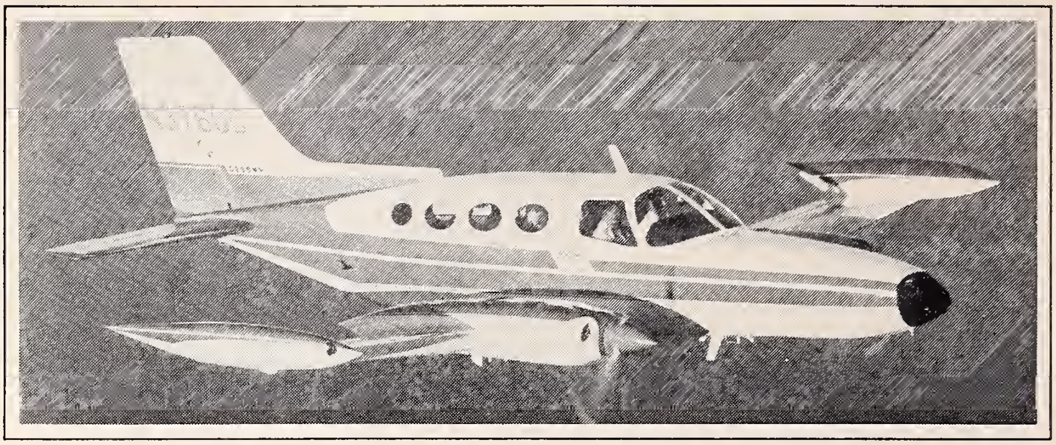

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1. Banov, L.: South. M. J. 57: 328-331 (March) 1964.

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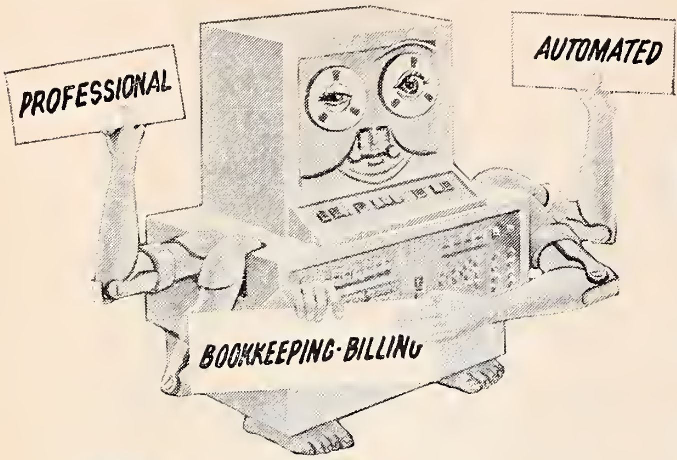

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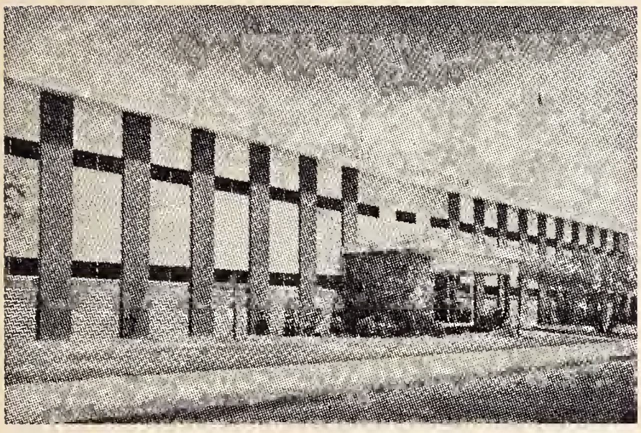

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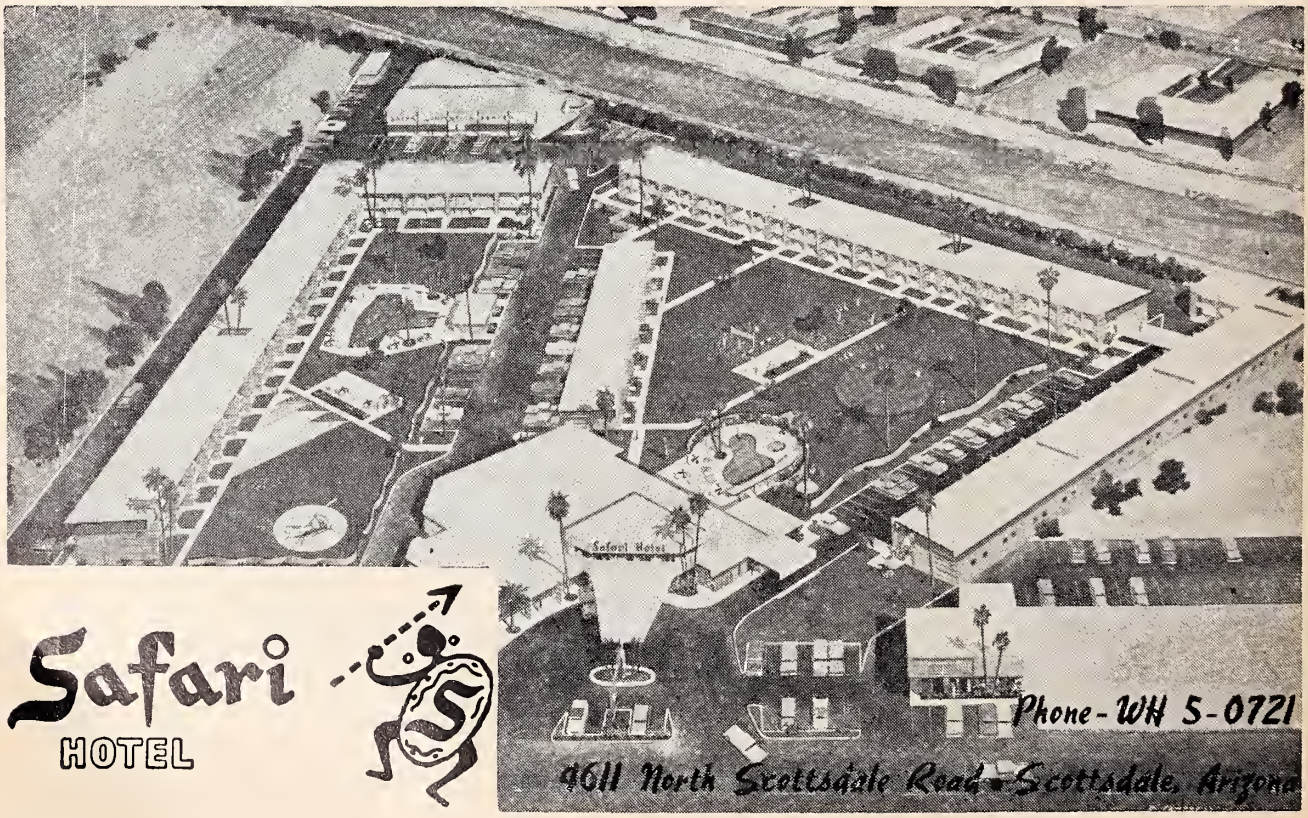

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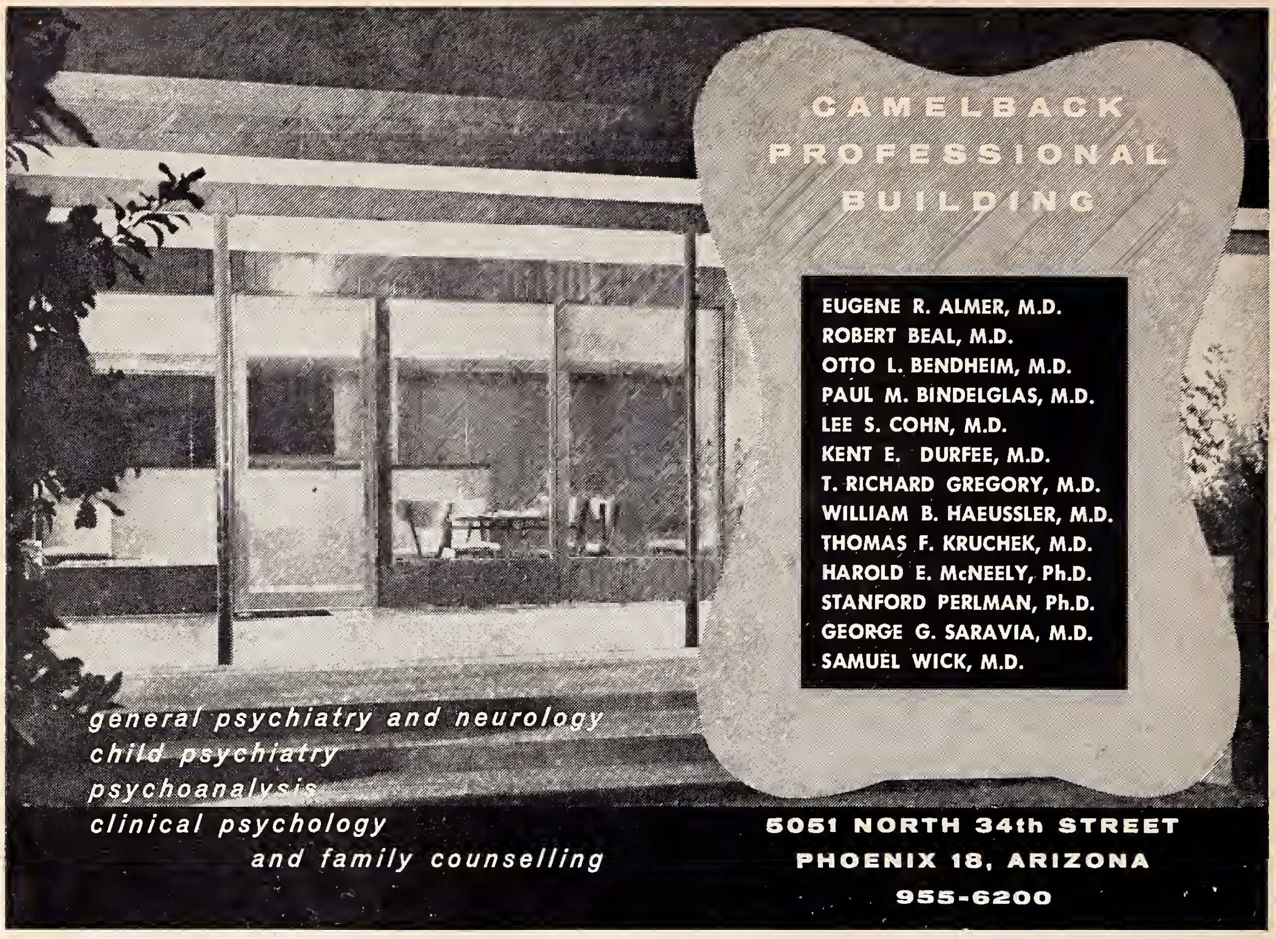

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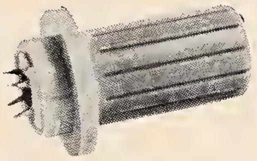

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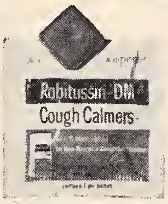

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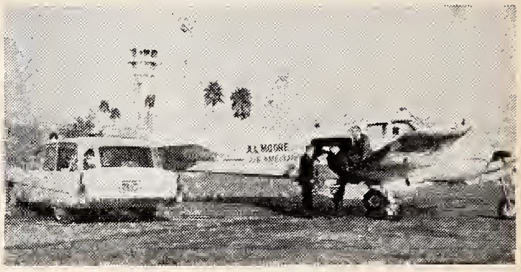

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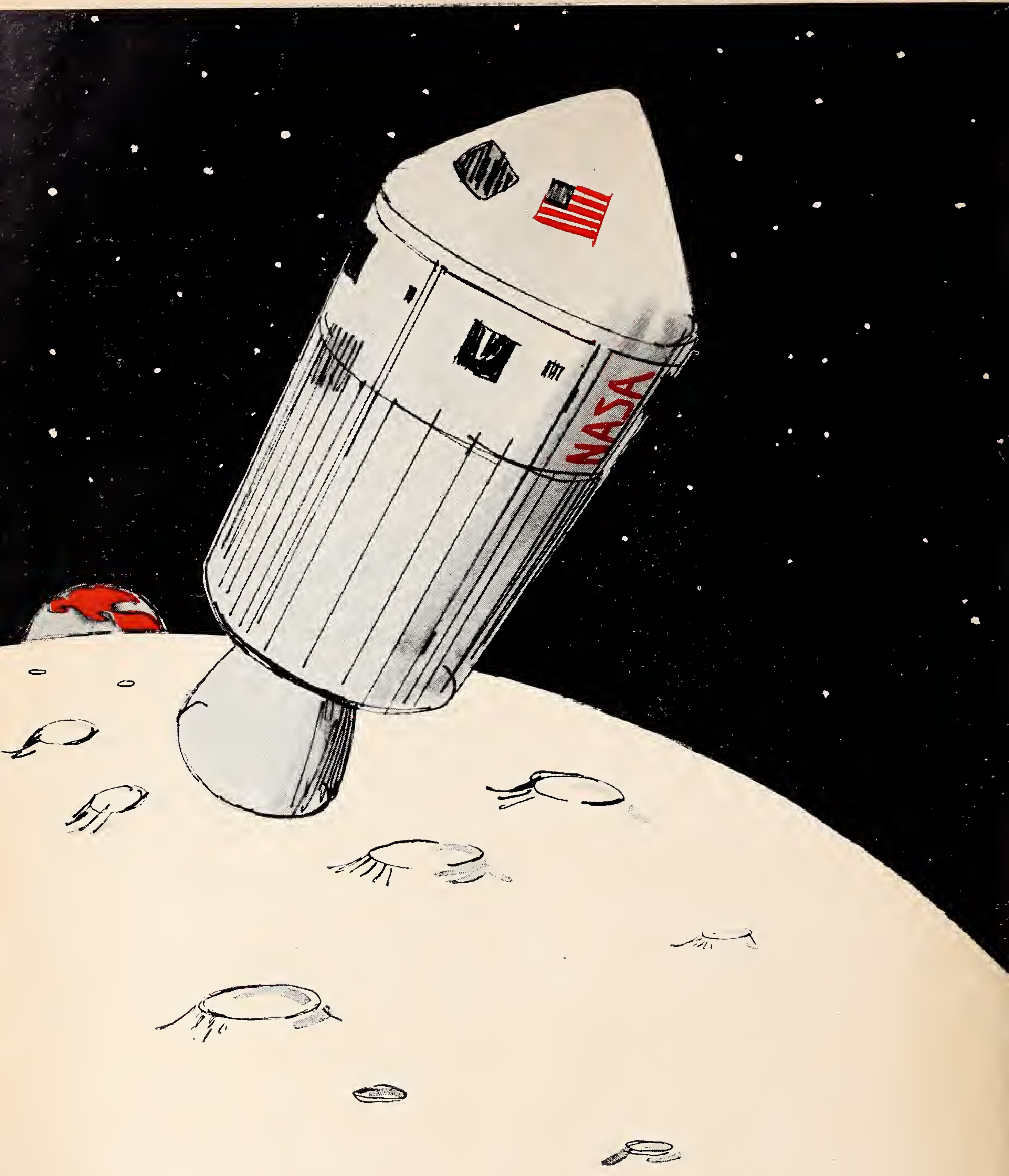

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